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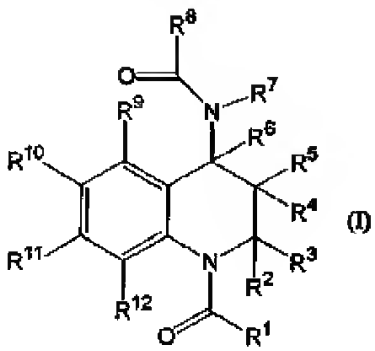
(54) Title: ANTI-INFLAMMATORY AGENT



(I)

(57) Abstract: An anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative represented by the formula (I): (I) (wherein R^1 represents hydrogen, (un)substituted lower alkyl, (un)substituted aryl, etc.; R^2 and R^3 are the same or different and each represents hydrogen, (un)substituted lower alkyl, etc.; R^4 and R^5 are the same or different and each represents hydrogen, etc.; R^6 represents hydrogen, etc.; R^7 represents (un)substituted cycloalkyl, (un)substituted aryl, etc.; R^8 represents (un)substituted lower alkyl, (un)substituted aryl, etc.; and R^9, R^{10}, R^{11}, and R^{12} are the same or different and each represents hydrogen, halogeno, (un)substituted lower alkyl, etc.) or a pharmacologically acceptable salt of the derivative.

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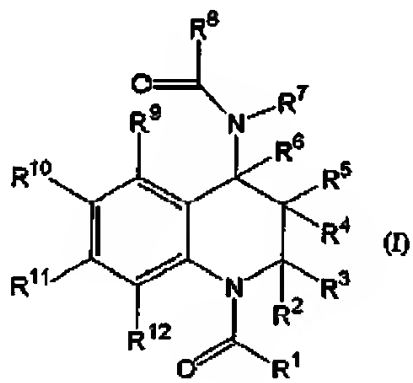
For acronyms and other abbreviation, see "Glossary of Acronyms and Abbreviation List" included in the preface of *PCT Gazette* issued periodically.

(57) Abstract:

Formula (1)



(I)

An anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative represented by the formula (I):
(wherein R^1 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl, and the like;
R^2 and R^3 are the same or different and each represents hydrogen, substituted or unsubstituted lower alkyl, and the like;
R^4 and R^5 are the same or different and each represent hydrogen, and the like;
R^6 represents hydrogen, and the like;
R^7 represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and the like;
R^8 represents substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl, and the like;
R^9, R^{10}, R^{11} and R^{12} are the same or different and each represents hydrogen, halogen, substituted or unsubstituted lower alkyl, and the like) or a pharmacologically acceptable salt of the derivative.

DESCRIPTION

Anti-Inflammatory Agent

Field of Invention

The present invention relates to an anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative, or 4-aminotetrahydroquinoline derivatives or a pharmacologically acceptable salt of the derivatives having an anti-inflammatory activity.

Background of Invention

Several 1-acyl-4-aminotetrahydroquinoline derivatives have been known until now (*Zhurnal Obshchei Khimii* ([*Russian Journal of General Chemistry*] Zh. Obshch. Khim.), vol. 44, p. 675 (1974); *Trudy Probleminiya Laboratoriya Khimii Vysokomolekulyarnye Soedineniya* ([*Proceedings of Laboratory Chemistry Problems on Polymer Science*] /Tr. Probl. Lab. Khim. Vysokomol. Soedin.), vol. 4, p. 5 (1996); *Zhurnal Organicheskoi Khimii* [*Russian Journal of Organic Chemistry*] Zh. Org. Khim.), vol. 3, p. 753 (1967)). Furthermore, the solid-phase synthesis of combinatorial libraries of 4-substituted quinolone derivatives is known as well (US 6,262,269).

As compounds having 4-aminotetrahydroquinoline skeleton, 1-acyl-4-aminotetrahydroquinoline derivatives are known as apolipoprotein AI promoters (Japanese Unexamined Patent Publication 2002-53557) as well as soluble beta-amyloid precursor protein promoters (WO 01/76629). 1-acyl-4-aminotetrahydroquinoline derivatives having trifluoromethyl in 6- or 7-position of tetrahydroquinoline ring are known as medications for respiratory tract inflammation as well as bronchial hypersensitivity (WO 93/19755). 1-acyl-4-aminotetrahydroquinoline derivatives having trifluoromethyl in 5-, 6- or 7-position of tetrahydroquinoline ring are known as bronchodilators as well as antihypertensives (WO 91/09031). 4-acylamino-tetrahydroquinoline derivatives are known as androgen receptor agonists or antagonists (WO 02/22585) or signal transduction inhibitors (WO 00/27802). 1-acyl-4 alkoxycarbonyl tetrahydroquinoline derivatives are known as cholesteryl ester transfer protein inhibitors (WO 02/22598). Finally, 1-acyl tetrahydroquinoline derivatives are known as STAT6 activity regulators (WO 02/79166).

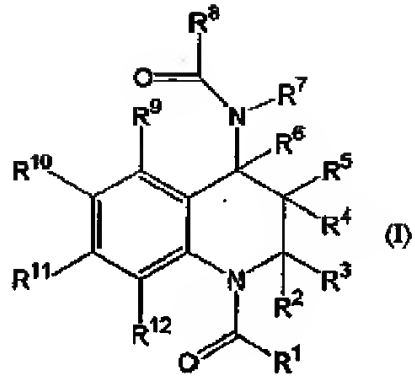
Invention Disclosure

The purpose of the present invention is in providing an anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative, or 4-aminotetrahydroquinoline derivatives or a pharmacologically acceptable salt and

the like of the derivatives having an anti-inflammatory activity.

The present invention relates to the following (1) through (31).

(1) Formula (I)



(I)

An anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative represented by the formula (I):

(wherein R^1 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, $CONR^AR^B$ (wherein R^A and R^B are the same or different and each represents hydrogen or substituted or unsubstituted lower alkyl, but R^A and R^B do not represent hydrogen at the same time), or NR^CR^D (wherein R^C and R^D are the same or different and each represents hydrogen, substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower aryl);

R^2 and R^3 are the same or different and each represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as R^A and R^B above);

R^4 and R^5 are the same or different and each represents hydrogen, halogen, nitro, hydroxyl, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or

unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, $CONR^{A2}R^{B2}$ (wherein R^{A2} and R^{B2} have the same meaning as R^A and R^B above), $NR^{C1}R^{D1}$ (wherein R^{C1} and R^{D1} have the same meaning as R^C and R^D above), OR^E (wherein R^E represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aromatic heterocyclic group), or $S(O)_nR^F$ (wherein *n* represents an integer 0 to 2 and R^F represents substituted or unsubstituted lower alkyl);

R^6 represents hydrogen, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A3}R^{B3}$ (wherein R^{A3} and R^{B3} have the same meaning as R^A and R^B above);

R^7 represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;

R^9, R^{10}, R^{11} and R^{12} are the same or different and each represents hydrogen, halogen, nitro, hydroxyl, mercapto, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, $CONR^{A4}R^{B4}$ (wherein R^{A4} and R^{B4} have the same meaning as R^A and R^B above), $NR^{C2}R^{D2}$ (wherein R^{C2} and R^{D2} have the same meaning as R^C and R^D above), OR^{E1} (wherein R^{E1} has the same meaning as R^E above), or $S(O)_{n1}R^{F1}$ (wherein *n*1 and R^{F1} have the same meaning as *n* and R^F above);

1-1) When R^1 represents lower alkyl or halogen-substituted lower alkyl;

1-1-1) and R^2 and R^3 above are the same or different and each represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above) (when, however, either one of R^2 or R^3 represents lower alkyl or halogen-substituted lower alkyl, the other one of R^2 or R^3 does not represent hydrogen);

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as R^A and R^B above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as R^C and R^D above);

1-1-2) and either one of R^2 or R^3 represents lower alkyl or halogen-substituted lower alkyl, the other one of R^2 or R^3 represents hydrogen; and

1-1-2-1) R^7 represents substituted or unsubstituted cycloalkyl or substituted or unsubstituted alicyclic heterocyclic group;

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above);

1-1-2-2) R^7 represents substituted or unsubstituted aryl or substituted or unsubstituted aromatic heterocyclic group;

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above);

1-2) When R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, $CONR^AR^B$ (wherein R^A and R^B have the same meaning as above), or NR^CR^D (wherein R^C and R^D have the same meaning as above);

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

(2) An anti-inflammatory agent as set forth in (1) above wherein R^4 and R^5 are hydrogen.

(3) An anti-inflammatory agent as set forth in (1) or (2) above wherein R^6 is hydrogen.

(4) An anti-inflammatory agent as set forth in (1) above wherein R^1 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d are the same or different and each represents hydrogen, substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower aryl, but do not represent hydrogen at the same time);
R^3, R^4, R^5 and R^6 each represents hydrogen;
At least two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen;
4-1) R^1 represents lower alkyl or halogen-substituted lower alkyl; and

4-1-1) R^2 represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted

or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as R^c and R^d above); or

4-1-2) R^2 represents lower alkyl or halogen-substituted lower alkyl;

4-1-2-1) R^7 represents substituted or unsubstituted cycloalkyl or substituted or unsubstituted alicyclic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); or

4-1-2-2) R^7 represents substituted or unsubstituted aryl or substituted or unsubstituted aromatic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); or

4-2) R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d have the same meaning as above);

R^2 represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted

or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above).

(5) An anti-inflammatory agent as set forth in (1) above wherein R^2 represents hydrogen, substituted or unsubstituted lower alkyl;
R^3, R^4, R^5 and R^6 each represents hydrogen;
R^7 represents substituted or unsubstituted aryl;
At least two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen, the other two are the same or different and each represents hydrogen, halogen, nitro, hydroxyl, lower alkyl, substituted or unsubstituted lower alkoxy; and
5-1) R^1 represents lower alkyl or halogen-substituted lower alkyl;

5-1-1) R^2 represents hydrogen, or substituted lower alkyl (excluding halogen-substituted lower alkyl); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; or

5-1-2) R^2 represents lower alkyl or halogen-substituted lower alkyl; and

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; or
5-2) R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group.

(6) An anti-inflammatory agent as set forth in (1), (2), or (3) above wherein R^9, R^{10}, R^{11} and R^{12} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower

alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^{E1} (wherein R^{E1} has the same meaning as above).

(7) An anti-inflammatory agent as set forth in (4) above wherein two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen, and the other two are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^{E1} (wherein R^{E1} has the same meaning as above).

(8) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S**, 4*R**), respectively.

(9) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R**, 4*R**), respectively.

(10) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*R*), respectively.

(11) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*S*), respectively.

(12) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*R*), respectively.

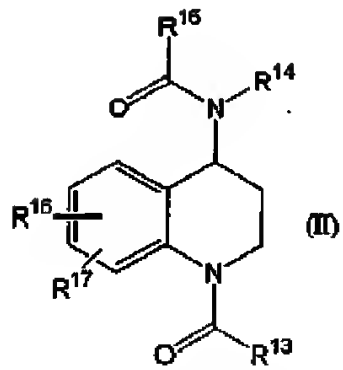
(13) An anti-inflammatory agent as set forth in (1), (2), (3), (4), (5), (6), or (7) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*S*), respectively.

(14) Usage of a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11), (12), or (13) above for the purpose of manufacturing an anti-inflammatory agent.

(15) A prevention and/ or a method for the treatment of inflammation which comprises the step to administer an effective dose of either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11), (12), or (13) above.

(16) A pharmaceutical composition having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (1), (2), (3), (4), (5), (6), (7), (8), (9), (10), (11), (12), or (13) above.

(17) Formula (II)



(II)

Either a 4-aminotetrahydroquinoline derivative represented by the formula (II):
(wherein R^{13} represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl,

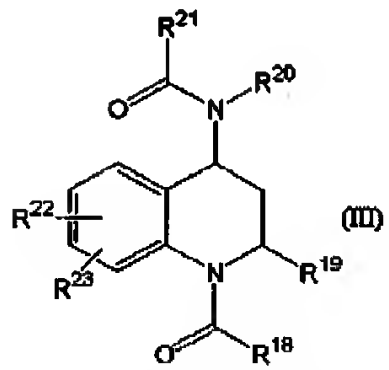
substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d have the same meaning as above);

R^{14} represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;

R^{15} represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); and

R^{16} and R^{17} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^E (wherein R^E has the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

(18) Formula (III)



(III)

A 4-aminotetrahydroquinoline derivative represented by the formula (III):

(wherein R^{18} represents substituted or unsubstituted aryl;

R^{19} represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted aromatic heterocyclic group, or $CONR^AR^B$ (wherein R^A and R^B have the same meaning as above);

R^{20} represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;
R^{21} represents substituted or unsubstituted cycloalkyl;
R^{22} and R^{23} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^E (wherein R^E has the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

(19) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18) above wherein R^{19} represents substituted or unsubstituted lower alkyl, and R^{22} and R^{23} each represents hydrogen.

(20) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18) or (19) above wherein R^{19} represents methyl.

(21) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19) or (20) above wherein R^{20} represents substituted or unsubstituted phenyl.

(22) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S**, 4*R**), respectively.

(23) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R**, 4*R**), respectively.

(24) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*R*), respectively.

(25) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*S*), respectively.

(26) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*R*), respectively.

(27) A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (18), (19), (20) or (21) above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*S*), respectively.

(28) An anti-inflammatory agent having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in (17), (18), (19), (20), (21), (22), (23), (24), (25), (26), or (27) above.

(29) Usage of a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (17), (18), (19), (20), (21), (22), (23), (24), (25), (26), or (27) above for the purpose of manufacturing an anti-inflammatory agent.

(30) A prevention and/ or a method for the treatment of inflammation which comprises the step to administer an effective dose of either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (17), (18), (19), (20), (21), (22), (23), (24), (25), (26), or (27) above.

(31) A pharmaceutical composition having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in (17), (18), (19), (20), (21), (22), (23), (24), (25), (26), or (27) above.

Hereafter, the compounds represented by Formulae (I), (II), and (III) will be referred to as Compounds (I), (II), and (III), respectively. Similarly, the compounds represented by other formula numbers will be referred to by the corresponding formula number.

The definitions of each group in Formulae (I), (II), and (III) are as follows:

Examples of halogen in halogen and halogen-substituted lower alkyl include fluorine, chlorine, bromine, and iodine.

Examples of lower alkyl include linear, branched, and/ or cyclic alkyl having carbon number of 1 to 10, more specifically, methyl, ethyl, propyl, isopropyl, cyclopropyl, cyclopropylmethyl, buthyl, sec-butyl, tert-butyl, cyclobutyl, pentyl, neopentyl, cyclopentyl, cyclopentylmethyl, hexyl, cyclohexyl, cyclohexylmethyl, heptyl, cycloheptyl, octyl, cyclooctyl, nonyl, decyl, cyclodecyl, and the like.

Cycloalkyl represents the cyclic lower alkyls mentioned in the definition above, and examples include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclodecyl, and the like.

The lower alkyl portion of lower alkoxy, lower alkoxycarbonyl, lower alkoxycarbonylamino and lower alkylthio has the same meaning as the abovementioned lower alkyl.

Examples of lower alkanoyl portion in lower alkanoyl and lower alkanoylamino include linear, branched, and/ or cyclic alkanoyl having carbon number of 1 to 10, more specifically, formyl, acetyl, propionyl, isopropionyl, butyryl, isobutyryl, caproyl, cyclopentanecarbonyl, cyclopentylmethylcarbonyl, hexanoyl, heptanoyl, octanoyl, decanoyl, and the like.

Examples of lower alkenyl include linear, branched, and/ or cyclic alkenyl, alkadienyl, alkatrienyl and the like having carbon number of 2 to 10, more specifically, vinyl, aryl, 1-propenyl, 2-butenyl, 3-butenyl, 4-pentenyl, 2-(1-cyclohexenyl)ethyl, 6-octenyl, 2,6-octadienyl, 2,4,6-octatrienyl, 6-decenyl, and the like.

Examples of lower alkynyl include linear or branched alkynyl having a carbon number of 2 to 6, more specifically, ethynyl, propargyl, 3-butinyl, 4-pentinyl, 5-hexinyl, and the like.

Examples of aryl include monocyclic, bicyclic, or tricyclic aryl having a carbon number of 6 to 14, more specifically, phenyl, naphthyl, indenyl, anthryl, and the like.

The aryl portion of aralkyl, aralkyloxy, aryloxy lower alkyl, aroyl, and arylamino has the same meaning as the abovementioned aryl.

The alkylene portion of aralkyl and aralkyloxy is equivalent to one hydrogen atom short of linear or branched alkyl group in the abovementioned definition of lower alkyl.

The aralkyl portion of aralkyl and aralkyloxy comprises bicyclic hydrocarbon that is bound with aryl in two positions of branched alkyl in the groups listed in the abovementioned definition of lower alkyl, and examples include, indanyl, 1,2,3,4-tetrahydronaphtyl, 6,7,8,9-tetrahydro-5H-benzocycloheptyl, and the like.

Styryl represents 1-phenylvinyl or 2-phenylvinyl.

Examples of aromatic heterocyclic group include 5-member or 6-member monocyclic aromatic heterocyclic group having at least one hetero atom selected from nitrogen atom, oxygen atom or sulfur atom, and bicyclic or tricyclic aromatic heterocyclic group wherein 3- to 8-member rings are condensed, or more specifically, furyl, thienyl, pyrrolyl, pyridine, pyrazinyl, oxazolyl, thiazolyl, pyridazinyl, pyrazolyl, tetrazolyl, triazolyl, oxadiazolyl, thiadiazolyl, quinolyl, isoquinolyl, benzothienyl, triazinyl, benzofuranyl, indoryl, quinolyl, purinyl, benzodioxolyl, benzoxazolyl, benzothiazolyl, imidazolyl, pyrimidinyl, benzoimidazolyl, 9,10,10-trioxo-9,10-dihydro-10λ^6-thioxantenyl, benzo[b]thiophenyl, 1,3-dioxo-1,3-dihydroisoindolyl, and the like.

The aromatic heterocyclic group portion of aromatic heterocyclicoxy lower alkyl has the same meaning as the abovementioned aromatic heterocyclic group.

Examples of alicyclic heterocyclic group include 5-member or 6-member monocyclic alicyclic heterocyclic group having at least one hetero atom selected from nitrogen atom, oxygen atom or sulfur atom, bicyclic or tricyclic alicyclic heterocyclic group wherein 3- to 8-member rings are condensed, and heterocyclic group wherein endocycle is partially unsaturated, or more specifically, tetrahydropyranyl, tetrahydrothiopyranyl, morpholinyl, morpholino, thiomorpholinyl, thiomorpholino, pyrrolidyl, piperazinyl, homopiperazinyl, piperidyl, homopiperidyl, tetrahydrofuranyl, tetrahydroquinolyl, tetrahydroisoquinolyl dihydrobenzofuranyl, 1,2,3,6-tetrahydropyridyl, 1,3-dioxolanyl, 1,3-dioxo-1H,3H-benzoisoquinolyl, and the like.

The heterocyclic group includes both aromatic heterocyclic group and alicyclic heterocyclic group.

The heterocyclic group portion of heterocyclic group lower alkyl has the same meaning as the abovementioned heterocyclic group.

The lower alkylene portion of halogen-substituted lower alkyl, heterocyclic lower alkyl, aryloxy lower alkyl, and aromatic heterocyclicoxy lower alkyl has the same meaning as one hydrogen atom short of linear or branched alkyl group in the abovementioned definition of lower alkyl.

The substituent of substituted lower alkyl is the same or different, and examples include halogen, cyano, carboxy, amino, nitro, hydroxy, mercapto, lower alkoxy, lower alkanoyl, lower alkanoylcarbonyl, aroyl, N-mono-lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl (wherein two lower alkyl portions of said N,N-di-lower alkylaminocarbonyl may be the same or different), lower alkanoyloxy, aralkyloxy, mono- or di-lower alkylamino (two lower alkyl portions of said di-lower alkylamino may be the same or different), lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, heterocyclic group, substituted-heterocyclic group (wherein substituent of said substituted-heterocyclic group has the same meaning as the substituent of substituted-heterocyclic group mentioned below), aryloxy, substituted-

aryloxy (wherein substituent of said substituted-aryloxy has the same meaning as the substituent of substituted-aryl mentioned below), aromatic heterocyclicoxy, substituted-aromatic heterocyclicoxy (wherein substituent of said substituted- aromatic heterocyclicoxy has the same meaning as the substituent of substituted-heterocyclic group mentioned below), and the like, all having carbon number of 1 to 3.

The lower alkyl portion of halogen, lower alkoxy, lower alkoxycarbonyl, N-mono lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl, mono- or di-lower alkylamino, lower alkylthio, lower alkylsulfinyl, and lower alkylsulfonyl, the lower alkanoyl portion of lower alkanoyl and lower alkanoyloxy, the aryl portion of aralkyloxy, aroyl and aryloxy, the aromatic heterocyclic group portion of heterocyclic group and aromatic heterocyclicoxy, and the alkylene portion of aralkyloxy are the same as above.

The substituent of substituted-lower alkoxy, substituted-lower alkanoyl, substituted-alkoxycarbonyl, substituted-lower alkanoylamino, substituted-lower alkoxycarbonylamino, substituted-lower alkylthio and substituted-cycloalkyl has the same meaning as the substituent of abovementioned substituted-lower alkyl.

The substituent of substituted-lower alkenyl and substituted-lower alkynyl is the same or different, and examples include halogen, cyano, carboxy, amino, nitro, hydroxy, mercapto, lower alkyl, aryl, substituted-aryl (wherein substituent of said substituted-aryl has the same meaning as the substituent of substituted-aryl mentioned below), aralkyl, heterocyclic group, lower alkanoyl, lower alkoxy, lower alkoxycarbonyl, lower alkanoyloxy, aroyl, aryloxy, aralkyloxy, substituted-aromatic heterocyclicoxy, N-mono-lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl (wherein two lower alkyl portions of said N,N-di-lower alkylaminocarbonyl may be the same or different), mono- or di-lower alkylamino (two lower alkyl portions of said di-lower alkylamino may be the same or different), lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, and the like, all having carbon number of 1 to 3.

The lower alkyl portion of halogen, lower alkyl, lower alkoxy, lower alkoxycarbonyl, lower alkylthio, lower alkylsulfinyl, and lower alkylsulfonyl, N-mono lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl, and mono- or di-lower alkylamino, the lower alkanoyl portion of lower alkanoyl and lower alkanoyloxy, the aryl portion of aryl, aralkyl, aralkyloxy, aroyl and aryloxy, the aromatic heterocyclic group portion of heterocyclic group and aromatic heterocyclicoxy, and the alkylene portion of aralkyl and aralkyloxy have the same meaning as above.

The substituent of substituted-aryl, substituted-aralkyl, substituted-aralkyloxy, substituted-aroyl, substituted-arylamino, substituted-styryl, substituted-heterocyclic group, substituted-alicyclic heterocyclic group and substituted-aromatic heterocyclic group is the same or different, and examples include halogen, cyano, carboxy, amino, nitro, hydroxy, mercapto, lower alkyl, substituted-lower alkyl (wherein the examples of substituent of said substituted-lower alkyl include, the same or different, hydroxyl, aryloxy, aromatic heterocyclic group, aromatic heterocyclicoxy, and the like all having carbon number of 1 to 3; the aryl portion of aryloxy as well as the aromatic heterocyclic group portion of aromatic heterocyclic group and aromatic heterocyclicoxy have the same meaning as above), lower alkenyl, lower alkynyl, aryl, heterocyclic group, aralkyl, lower alkanoyl, lower alkoxy, lower alkoxycarbonyl, lower alkanoyloxy, aroyl, aryleoxy, aralkyloxy, aromatic heterocyclicoxy, N-mono-lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl (wherein two lower alkyl portions of said N,N-di-lower alkylaminocarbonyl may be the same or different), mono- or di-lower alkylamino (two lower alkyl portions of said di-lower alkylamino may be the same or different), lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, and the like, all having carbon number of 1 to 3.

The lower alkyl portion of halogen, lower alkyl, lower alkoxy, lower alkoxycarbonyl, N-mono lower alkylaminocarbonyl, N,N-di-lower alkylaminocarbonyl, mono- or di-lower alkylamino, lower alkylthio, lower alkylsulfinyl, and lower alkylsulfonyl, the lower alkanoyl portion of lower alkenyl, lower alkynyl, lower alkanoyl and lower alkanoyloxy, the aryl portion of aryl, aralkyl, aralkyloxy, aroyl and aryloxy, the aromatic heterocyclic group portion of heterocyclic group and aromatic heterocyclicoxy, and the alkylene portion of aralkyl and aralkyloxy have the same meaning as above.

Examples of pharmacologically acceptable salt include alkali metal salt, such as sodium salt and potassium salt, alkali earth metal salt, such as magnesium salt and calcium salt, ammonium salt such as aluminum salt, ammonium salt, and tetramethylammonium salt, organic amine addition salt, such as morpholine salt and piperidine salt, amino acid addition salt, such as lysine salt, glycine salt, and phenylalanine salt, inorganic acid salt, such as hydrochloric acid salt, sulfuric acid salt, and phosphoric acid salt, and organic acid salt, such as acetic acid salt, maleic acid salt, fumaric acid salt, tartaric acid salt, citric acid salt, succinic acid salt, benzoic acid salt, methanesulfonic acid salt, lactic acid salt, gluconic acid salt, embonic acid salt, glucuronic acid salt, and benzenesulfonic acid salt.

Some of Compounds (I), (II), (III), as well as pharmacologically acceptable salt of the compounds, may contain various types of stereoisomers, optical isomers, positional isomers, tautomer, and the like.

All possible isomers as well as mixtures of isomers may be used for the anti-inflammatory agent of the present invention, and any mixture ratio may be used.

2*S* and 2*R* used for transcribing the absolute configuration of the present description represent the absolute configuration of the 2-position in the tetrahydroquinoline structure. More specifically, the absolute configuration of carbons, which bind with R^2 and R^3 in Compound (I), and the absolute configuration of carbons, which bind with R^{19} in Compound (III). Similarly, 4*S* and 4*R* used for transcribing the absolute configuration represent the absolute configuration of the 4-position in the tetrahydroquinoline structure. More specifically, the absolute configuration of carbons, which bind with $-NR^7C(O)R^8$ in Compound (I), the absolute configuration of carbons, which bind with $-NR^{14}C(O)R^{15}$ in Compound (II), and the absolute configuration of carbons, which bind with $-NR^{20}C(O)R^{21}$ in Compound (III).

(2*S** and 4*R**) used for transcribing the absolute configuration of the present description represent (2*S* and 4*R*), (2*R* and 4*S*) or the mixture in any ratio of (2*S* and 4*R*) and (2*R* and 4*S*) in the abovementioned definition of the absolute configuration. Similarly, (2*R** and 4*R**) represent (2*R* and 4*R*), (2*S* and 4*S*) or the mixture in any ratio of (2*R* and 4*R*) and (2*S* and 4*S*) in the abovementioned definition of the absolute configuration.

Compounds (I), (II), (III), as well as pharmacologically acceptable salt of the compounds may exist as a water adduct or a various types of solvent adduct. The said adducts may be used for the anti-inflammatory agent of the present invention, and the present invention comprises the said adduct as well.

The present invention comprises compounds, wherein one or more atoms involved in Compound (I), Compound (II), or Compound (III) are labeled by an isotope. The compounds that incorporate radioisotopes, such as ^3H and ^{14}C, among other isotopes are useful for investigating the histological distribution of compounds.

The terminology of isotopes utilized in the present description indicates atoms having a valence and a nuclear number different from those generally found in nature. Examples of isotopes of compounds in the present invention include ^2H, ^3H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, and the like.

Examples of inflammatory disease that are treated by an anti-inflammatory agent include diseases selected from a group of diseases consisting of asthma, arthritis, pyrexia, influenza, inflammatory bowel disease, Chron's disease, emphysema, acute dyspnea syndrome, bronchitis, chronic pulmonary atresia, organ transplant toxicosis, cachexia, allergic reaction, allergic rhinitis, chronic rhinitis, hay fever, conjunctivitis, eczema, urticaria, psoriasis, cutaneous candidiasis, chronic rheumatic arthritis, adult T-cell leukemia (ATL and the like), allergic contact dermatitis, cancer, tissue ulceration, digestive ulcer, gastritis,

ulcerative colitis, recurrent gastrointestinal lesion, synovitis, gout, ankylosing spondylitis, peridontitis, subepidermal blister disease, joint implant loosening, atherosclerosis, aortic aneurysm, periarteritis nodosa, cerebral ischemia, neuralgia, neurodegenerative disease, autoimmune disease, pain, gingivitis, amyotrophic lateral sclerosis, multiple sclerosis, macular dystrophy, conjunctivitis, wound healing disorder, sprains and contusions of muscle or joint, tendonitis, skin disease, severe myasthenia, polymyositis, myositis, synovial capsulitis, fever, diabetes, tumorous invasion, tumor growth, tumor metastasis, corneal scar, scleritis, immunodeficiency disease, ichorrhemia, hypoprothrombinemia, thyroiditis, sarcoidosis, Behcet's syndrome, hypersensitivity, renal disease, rickettsial infection, protozoan disease, and septicemic shock, as well as inflammatory diseases other than the above with which eosinophil is believed to be involved (for example, Churg-Strauss Syndrome, Kimura's Disease, pemphigus, pemphigoid, eosinophilic fasciitis, eosinophilic leukemia, recurrent angioedema with eosinophilia, and the like).

Compound (I), Compound (II), or Compound (III) may be administered in combination with one or more of other types of therapeutic agent.

Preferred examples of Compound (I), Compound (II), and Compound (III) include groups of compound described in Table 1-1 through 1-38, Table 2, or Table 3-1 through 3-7 described below, among which particularly preferred examples of compound include, Compound 1-4, Compound 1-7, Compound 1-8, Compound 1-11, Compound 1-18, Compound 1-20, Compound 1-24, Compound 1-63, Compound 1-133, Compound 1-155, Compound 1-217, Compound 1-221, Compound 1-223, Compound 1-225, Compound 1-231, Compound 1-236, Compound 2-2, Compound 3-1, Compound 3-3, Compound 3-15, Compound 3-23, Compound 3-28, Compound 3-35, Compound 3-36, Compound 3-37, and Compound 3-39.

The manufacturing methods of Compound (I), Compound (II), and Compound (III) are as follows:

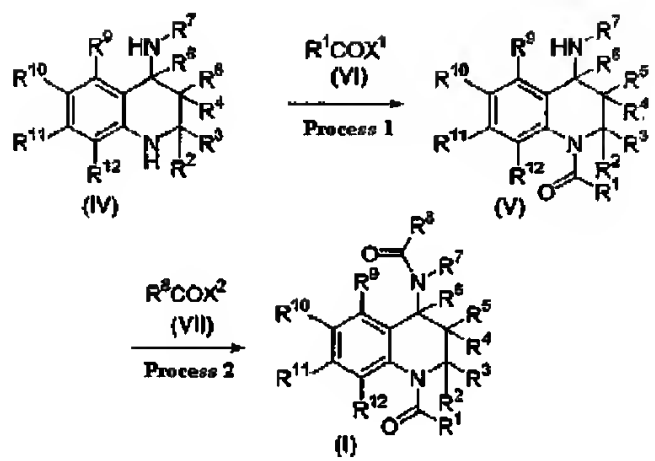
In the manufacturing methods presented below, if the defined groups change in the reaction condition, or if implementation of the method is inappropriate, the compounds can be easily manufactured using the methods commonly used in organic synthetic chemistry, such as protection and deprotection of functional groups (see, for example, "*Protective Groups in Organic Synthesis*" by T. W. Greene (John Wiley & Sons, Inc.) (1999)). Furthermore, the order of reaction process, such as an introduction of substituent, may be changed as necessary.

Some of the compounds of Compound (I) may be commercially available. Additionally, the compounds can also be obtained by using publicly known methods (see *Zhurnal Obshchei Khimii* ([*Russian Journal of General Chemistry*] Zh. Obshch. Khim.), vol. 44, p. 675 (1974); *Trudy Probleminiya*

Laboratoriya Khimii Vysokomolekulyarnye Soedineniya ([*Proceedings of Laboratory Chemistry Problems on Polymer Science*] /Tr. Probl. Lab. Khim. Vysokomol. Soedin.), vol. 4, p. 5 (1996); *Zhurnal Organicheskoi Khimii* [*Russian Journal of Organic Chemistry*] Zh. Org. Khim.), vol. 3, p. 753 (1967); and WO 98/34115).

Furthermore, Compound (I), Compound (II), and Compound (III) can be synthesized from publicly known compounds using, for example, the manufacturing method 1 to 3 below:

Manufacturing Method 1



(wherein X^1 and X^2 each represents hydroxyl, halogen, azide, alkoxy, alkanoyl, or aroyl, and R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} have the same meaning as above)

The Compound (V) or Compound (I) can be synthesized by amidating Compound (IV) or Compound (V) with a carboxylic acid derivative (VI). A vast number of methods, such as reaction between amine and carboxylic acid (X^1: hydroxyl), acid halide (X^1: halogen), or acid anhydride (X^1: alkanoyl or aroyl), as well as ester-amide exchange between amine and ester (X^1: alkoxy) are known as amidation methods (see "*Experimental Chemistry Series, 4th ed.*," Vol. 22, p. 128 (1990), and the like), and Compound (V) or Compound (I) can be synthesized by using one of the appropriate method above.

[Process 1]

The Compound (IV) comprising the raw material can be created using a publicly known method (see *Zhurnal Obshchei Khimii* ([*Russian Journal of General Chemistry*] Zh. Obshch. Khim.), vol. 44, p.

675 (1974); US 6,262,169; JP Unexamined Patent Publication 2002-53557; WO 01/76629; WO 93/19755; WO 02/22598, and the like).

For instance, Compound (V) can be obtained by reacting Compound (IV) with one equivalent weight to an overly excessive amount of acid halide in an inert solvent, a mixture of inert solvent and water, or an absence of solvent, in the presence of one equivalent weight to an excessive amount of base, as necessary, at a boiling temperature of solvent used from -78 degrees Celsius, for 5 minutes to 12 hours. Preferably, the reaction should take place at 0 degrees Celsius to room temperature, and 1 to 2 equivalent weight of base and 1 to 1.5 equivalent weight of acid halite should be used.

As an example of reaction between Compound (IV) and carboxylic acid, Compound (IV) can be reacted with a condensing agent as well as one equivalent weight to an overly excessive amount of carboxylic acid, in an inert solvent, under he existence of one equivalent weight to an excessive amount of base, as necessary, at a boiling temperature of solvent used from -78 degrees Celsius to obtain Compound (V). Preferably, the reaction should be performed at 0 degrees Celsius to room temperature, and 1 to 2 equivalent weight of the base should be used.

Examples of a condensing agent include dicyclohexylcarbodiimide, N-ethyl-N-(3-dimethylaminopropyl)carbodiimide, activated molecular sieves, carbonyldiimidazol, 2-etoxy-1-etoxycarbonyl-1,2-dihydroquinoloine, diethyl cyanophosphonate, diphenylphosphorazide, and the like.

Examples of an inert solvent include tetrahydrofuran, dioxane, acetone, ethyl acetate, diethyl ether, ethylene glycol, triethylene glycol, glyme, diglyme, methanol, ethanol, 2-propanol, buthanol, dichloromethane, chloroform, benzene, toluene, dimethylformamide, dimethylsulfoxide, dimethylimidazol, dimethylpropylurea, hexane, and the like.

Examples of a base include sodium hydroxide, potassium carbonate, sodium hydrogen carbonate, barium hydroxide, cesium carbonate, potassium hydroxide, sodium methoxide, potassium ethoxide, lithium hydroxide, lithiumhexamethyldisilazan, sodium hydride, potassium hydride, butyllithium, lithiumdiisopropylamide, potassium tert-butoxide, triethylamine, diisopropylethylamine, tributylamine, dicyclohexylmethylamine, N-methylmorpholine, pyridine, 2,6-di-tert-butylpyridine, N- methylpiperidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4,3,0]non-5-ene, 4,4-dimethylaminopyridine, Amberlyst A21 (by Rohm & Haas Co.), AG 1-X8 (by Bio-Rad Laboratories), poly (4-vinylpyridine), morpholinomethyl polystyrene, and the like.

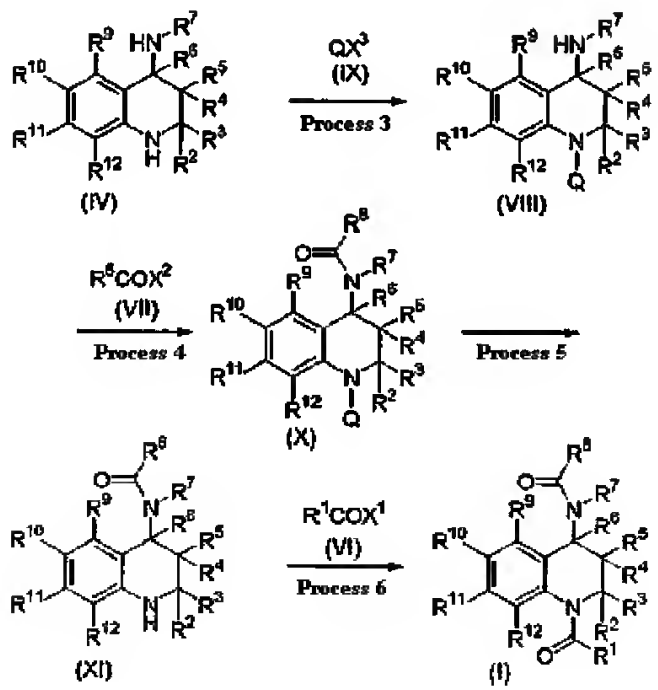
[Process 2]

The Compound (I) can be obtained by the same method as Process 1 or other publicly known methods (see, for example, *Zhurnal Obshchei Khimii* ([*Russian Journal of General Chemistry*] Zh. Obshch. Khim.), vol. 44, p. 675 (1974); US 6,262,269; JP Unexamined Patent Publication 2002-53557; WO 93/19755; WO 01/76629; WO 02/22598, and the like).

Compound (I) can be synthesized by amidation of, for example, Compound (V) and a carboxylic acid derivative.

For instance, Compound (I) can be obtained by reacting Compound (V) with one equivalent weight to an overly excessive amount of acid halide (X^2: halogen) in an inert solvent, a mixture of inert solvent and water, or an absence of solvent, in the presence of one equivalent weight to an excessive amount of base, as necessary, at a boiling temperature of solvent used from -78 degrees Celsius, for 5 minutes to 12 hours. Preferably, the reaction should be performed at 50-90 degrees Celsius, and 1 to 8 equivalent weight of the base and 2 to 8 equivalent weight of the acid halide should be used.
Examples of an inert solvent and a base are the same as the examples listed in Process 1.

Manufacturing Method 2



(wherein QX^3 represents a reagent that introduces a protective group suitable for protecting the amino group, and X^1, X^2, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} have the same meaning as above)

Compound (I) can also be synthesized by first reacting a proper protective group-introducing reagent (IX) to Compound (IV) comprising the raw material to protect the nitrogen atom in 1-position and create Compound (VIII). The same method as in Process 2 above can be used on Compound (VIII) to create Compound (X), and then Compound (XI) can be prepared by performing an appropriate deprotection reaction on the protective group used. Finally, Compound (I) can be synthesized by employing the same method used in Process 1 above on Compound (XI).

[Process 3]

Many examples of amino-protecting group, reactions for introducing protective group, and reagents for introducing protective group are well known (see, for example, *Protective Groups in Organic Synthesis*" by T. W. Greene (John Wiley & Sons, Inc.) (1999)), and any appropriate method thereof can be used to synthesize Compound (VIII).

For instance, the amino group in 1-position of Compound (IV) can be protected by reacting Compound (IV) with 1 to 10 equivalent weight of a protective group-introducing reagent (IX) in the presence of a catalytic amount to an excessive amount of base, as needed, in an inert solvent or an absence of solvent.

Examples of an inert solvent include tetrahydrofuran, dioxane, acetone, ethyl acetate, diethylether, ethyleneglycol, triethyleneglycol, glyme, diglyme, methanol, ethanol, 2-propanol, butanol, dichloromethane, chloroform, benzene, toluene, dimethylformamide, dimethylsulphoxide, and the like.

Examples of a base include sodium hydroxide, potassium carbonate, sodium hydrogen carbonate, barium hydroxide, cesium carbonate, potassium hydroxide, sodium methoxide, potassium ethoxide, lithium hydroxide, lithiumhexamethyldisilazan, sodium hydride, potassium hydride, butyllithium, lithiumdiisopropylamide, potassium tert-butoxide, triethylamine, diisopropylethylamine, tributylamine, dicyclohexylmethylamine, N-methylmorpholine, pyridine, N- methylpiperidine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4,3,0]non-5-ene, 4,4-dimethylaminopyridine, Amberlyst A21 (by Rohm & Haas Co.), AG 1-X8 (by Bio-Rad Laboratories), poly (4-vinylpyridine), morpholinomethyl polystyrene, and the like.

Examples of a protective group-introducing reagent include methyl chloroformate, ethyl chloroformate, benzyl chloroformate, 9-fluorenylmethyloxycarbonyl chloride, 9-

fluorenylmethyloxycarbonyl azide, trichloroethoxycarbonyl chloride, trimethylsilylethoxycarbonyl chloride, tert-butyloxycarbonyl chloride, di-tert-butyldicarbonate, acetyl chloride, benzoyl chloride, benzyl chloride, para-methoxybenzyl chloride, arylbromide, triisopropylsilyl chloride, trityl chloride, and the like. Preferred protective group-introducing reagent is benzyl chloroformate.

[Process 4]

The Compound (X) can be synthesized by an amidation of Compound (VIII) obtained in Process 3 above and a carboxylic acid derivative (VII).

For instance, Compound (X) can be obtained by reacting Compound (VIII) with one equivalent weight to an overly excessive amount of acid halide (X^2: halogen) in an inert solvent, a mixture of inert solvent and water, or an absence of solvent, in the presence of one equivalent weight to an excessive amount of base, as necessary, at a boiling temperature of solvent used from -78 degrees Celsius, for 5 minutes to 12 hours. Preferably, the reaction should be performed at room temperature, and 1 to 2 equivalent weight of the base and 1 to 1.5 equivalent weight of the acid halide should be used. Examples of an inert solvent and a base are the same as the examples listed in Process 1.

[Process 5]

Many examples of deprotection of amino-protecting group are well known (see, for example, *Protective Groups in Organic Synthesis*" by T. W. Greene (John Wiley & Sons, Inc.) (1999)), and any appropriate method thereof can be used to synthesize Compound (XI).

Deprotection of the protective group of amino group in 1-position of Compound (X) can be performed, for example when the protective group is benzyloxycarbonyl, by reacting Compound (X) in an inert solvent at a boiling temperature of solvent used from 0 degrees Celsius for 5 minutes to 72 hours, in the presence of hydrogen having 1 to 90 atmospheric pressure, using a catalyst having 1 to 100 weight percent, and adding acid as necessary.

Examples of an inert solvent include tetrahydrofuran, dioxane, acetone, ethyl acetate, diethylether, ethyleneglycol, triethyleneglycol, glyme, diglyme, methanol, ethanol, 2-propanol, butanol, dichloromethane, chloroform, dimethylformamide, dimethylsulphoxide, and the like.

Examples of a catalyst include palladium, palladium hydroxide, platinum, chlorotris(triphenylphosphine)rhodium (I), hydridocarbonyltris(triphenylphosphine)rhodium (I), rhodium acetate (II), ruthenium acetate (II), chlorohydridotris(triphenylphosphine)ruthenium (II), hydridocarbonyltris(triphenylphosphine)iridium (I), hexachloroplatinic acid (IV), potassium

hexacyanocobaltate (III) and the like. The catalyst may be supported by an active carbon, polyethylenimine and the like, as needed.

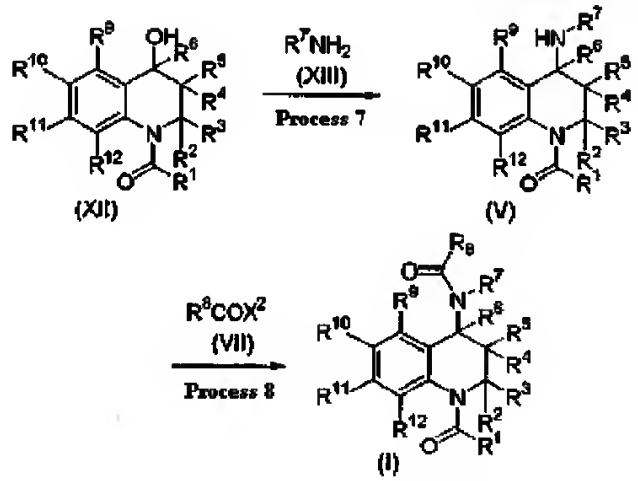
Examples of acid include formic acid, acetic acid, isovaleric acid, benzoic acid, butanoic acid, hydrochloric acid, sulfuric acid, trifluoromethanesulphonic acid, trifluoroacetic acid, ammonium chloride, and the like.

Preferred synthesis method of Compound (XI) is reacting Compound (X) in ethanol, in the presence of hydrogen having 1 to 3 atmospheric pressure, using 10 % palladium carbon having 3 to 10 weight percent as a catalyst, adding 2 to 10 equivalent weight of formic acid, and at a temperature of 30-45 degrees Celsius for 10 to 12 hours.

[Process 6]

The Compound (I) can be synthesized by an amidation of Compound (XI) using the same method described in Process 1 above. Compound (XI) comprising the raw material can be prepared by Process 5 above as well as a publicly known method (see WO 02/22585).

Manufacturing Method 3



(wherein X^2, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11} and R^{12} have the same meaning as above)

[Process 7]

Compound (XII) can be obtained by a publicly known method (see, for example, *"Tetrahedron"* vol. 53, p. 9715 (1997); *Journal of the American Chemical Society (J. Am. Chem. Soc.)*, vol. 71, p. 1901 (1949); *Journal of the American Chemical Society (J. Am. Chem. Soc.)*, vol. 71, p. 1906 (1949); *Journal*

of the American Chemical Society (J. Am. Chem. Soc.), vol. 74, p. 4513 (1952); *Journal of Chemical Society (J. Chem. Soc.)*, p. 4166 (1957); *Journal of Chemical Society (J. Chem. Soc.)*, p. 4174 (1957), and the like). Compound (XII) can also be easily induced from a well-known compound by reducing corresponding ketone if R^6 of Compound (XII) is hydrogen.

Compound (V) can be obtained by activating Compound (XII) using an appropriate method, and then reacting the activated Compound (XII) with Compound (XIII).

Many examples of alkylation of amines using alcohol are known. Such examples include a method wherein alcohol is converted to iodine using an iodinated trimethylsilane, and the said iodine is reacted with amine without isolation (see *Tetrahedron Letters (Tetrahedron Lett.)*, vol. 38, p. 2673 (1997)]; a method utilizing an applied Mitsunobu Reaction (see *Tetrahedron Letters (Tetrahedron Lett.)*, vol. 38, p. 5831 (1997)); a method using tosyl chloride (see "*Synthesis*," p. 665 (1974)), and the like.

For instance, Compound (V) can be prepared by reacting Compound (XII) with trimethylsilane iodide in an inert solvent at a boiling temperature of solvent used from 0 degrees Celsius, and then with Compound (XIII) in the presence of one equivalent weight to an overly excessive amount of the base.

Examples of an inert solvent include tetrahydrofuran, dioxane, acetone, ethyl acetate, diethylether, ethyleneglycol, triethyleneglycol, glyme, diglyme, methanol, ethanol, 2-propanol, butanol, dichloromethane, chloroform, benzene, toluene, dimethylformamide, dimethylimidazole, dimethylpropyleneurea, hexane, dimethylsulphoxide, and the like. Preferred inert solvent is dichloromethane.

Examples of a base include sodium hydroxide, potassium carbonate, sodium hydrogen carbonate, barium hydroxide, cesium carbonate, potassium hydroxide, sodium methoxide, potassium ethoxide, lithium hydroxide, lithiumhexamethyldisilazan, sodium hydride, potassium hydride, butyllithium, lithiumdiisopropylamide, potassium tert-butoxide, triethylamine, diisopropylethylamine, tributylamine, dicyclohexylmethylamine, N-methylmorpholine, pyridine, N- methylpiperidine, 2,6-di-tert-butylpyridine, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4,3,0]non-5-ene, 4,4-dimethylaminopyridine, Amberlyst A21 (by Rohm & Haas Co.), AG 1-X8 (by Bio-Rad Laboratories), poly (4-vinylpyridine), morpholinomethyl polystyrene, and the like. Preferred base is barium hydroxide.

[Process 8]

Using the same method described in Process 2 above, Compound (I) can be synthesized from Compound (V).

Intermediates as well as target compounds in each manufacturing method above can be isolated or refined using a separation and refinement method, for example, filtration, extraction, washing, drying, concentration, recrystallization, various types of chromatographies, and the like that is regularly used in the field of organic synthetic chemistry. Furthermore, the intermediates and target compounds can be refined by a refinement method that is regularly used in general parallel synthesis, for example, that uses a scavenger resin or an ion exchange resin. The intermediate can also be subjected to a subsequent reaction without refinement in particular. When an intermediate or a target compound can form a salt with an acid or a base, it can be refined as a salt. When a final product is obtained in isolated form, the final product can be isolated and refined after dissolving or suspending in a proper solvent and adding an acid or a base to form a salt. As an alternative method, a final product that was obtained in a form of salt can be converted into an isolated form, and then converted further into a target salt.

Concrete examples of Compound (I), Compound (II), and Compound (III) obtained by abovementioned manufacturing methods are shown in Table 1-1 through 1-38, Table 2, and Table 3-1 through 3-7, respectively; however, the scope of present invention is not limited to the compounds thereof. Compounds 1-1 through 1-209 are commercially available.

Table 1-1

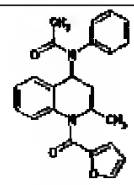
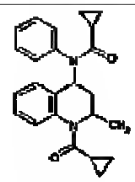
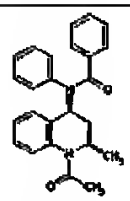
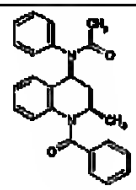
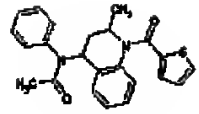
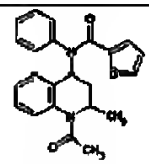
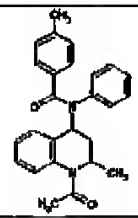
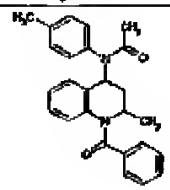
Compound 1-1		N-[1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-2		N-(1-cyclopropanecarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylcyclopropanecarboxamide
Compound 1-3		N-[(2*S**, 4*R**)-1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylbenzamide
Compound 1-4		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-5		N-{2-methyl-1-(2-tenoyl)-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide
Compound 1-6		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylthiophene-2-carboxamide
Compound 1-7		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-methylbenzamide
Compound 1-8		N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(p-tolyl)acetamide

Table 1-2

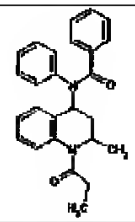
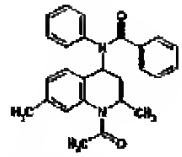
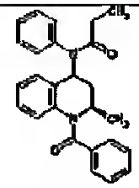
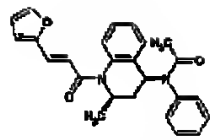
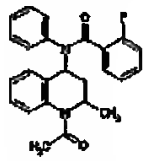
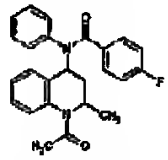
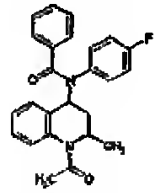
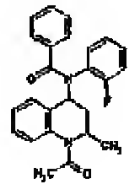
Compound 1-9		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylbenzamide
Compound 1-10		N-(1-acetyl-2,7-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylbenzamide
Compound 1-11		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpropionamide
Compound 1-12		N-{(2*S**, 4*R**)-1-[3-(2-furyl)acryloyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide
Compound 1-13		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-fluorobenzamide
Compound 1-14		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-fluorobenzamide
Compound 1-15		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(4-fluorophenyl)benzamide
Compound 1-16		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(2-fluorophenyl)benzamide

Table 1-3

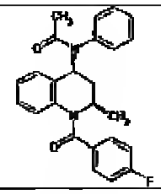
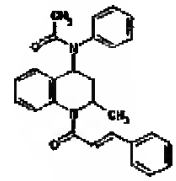
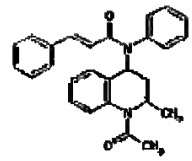
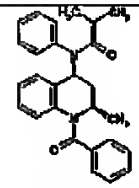
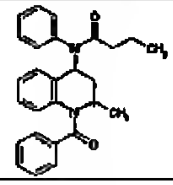
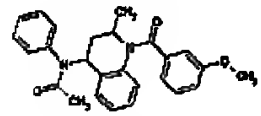
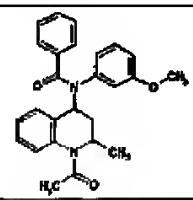
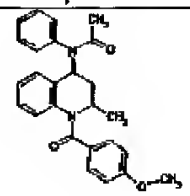
Compound 1-17		N-[(2*S**, 4*R**)-1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-18		N-(1-cinnamoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylacetamide
Compound 1-19		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylcinnamamide
Compound 1-20		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylisobutylamide
Compound 1-21		N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylbutylamide
Compound 1-22		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-23		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-methoxyphenyl)benzamide
Compound 1-24		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide

Table 1-4

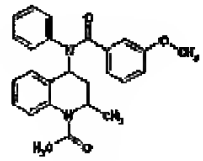
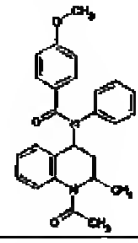
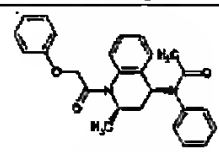
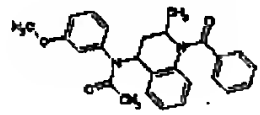
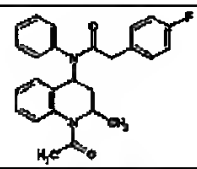
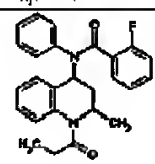
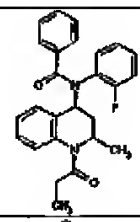
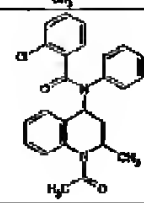
Compound 1-25		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-methoxybenzamide
Compound 1-26		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-methoxybenzamide
Compound 1-27		N-[(2*S**, 4*R**)-1-phenoxyacetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-28		N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-methoxyphenyl)acetamide
Compound 1-29		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-fluorophenylacetamide
Compound 1-30		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-fluorobenzamide
Compound 1-31		N-(2-fluorophenyl)-N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)benzamide
Compound 1-32		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-chlorobenzamide

Table 1-5

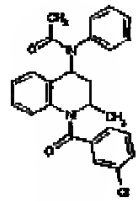
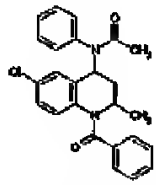
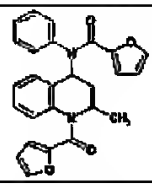
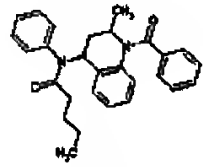
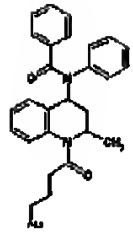
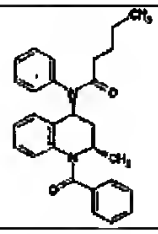
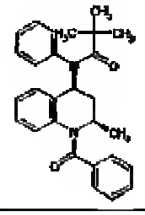
Compound 1-33		N-[1-(3-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-34		N-(1-benzoyl-6-chloro-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylacetamide
Compound 1-35		N-[1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylfuran-2-carboxamide
Compound 1-36		N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N- phenylvaleramide
Compound 1-37		N-(2-methyl-1-valeryl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylbenzamide
Compound 1-38		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylvaleramide
Compound 1-39		N-[(2*S**, 4*R**)-1-benzoyl -2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpivalamide

Table 1-6

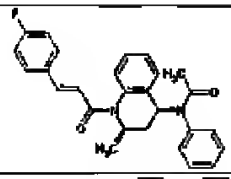
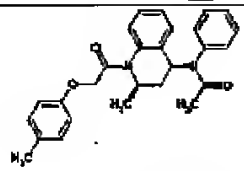
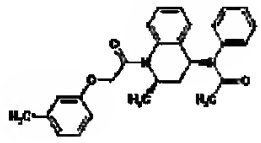
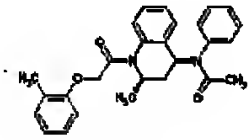
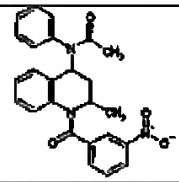
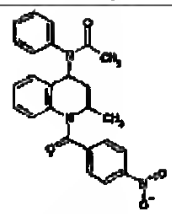
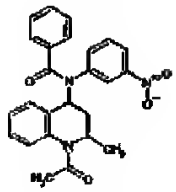
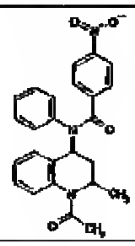
Compound 1-40		N-[(2*S**, 4*R**)-1-(4-fluorocinnamoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-41		N-{(2*S**, 4*R**)-1-[(4-methylphenoxy)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide
Compound 1-42		N-{(2*S**, 4*R**)-1-[(3-methylphenoxy)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide
Compound 1-43		N-{(2*S**, 4*R**)-1-[(2-methylphenoxy)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide
Compound 1-44		N-[2-methyl-1-(3-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-45		N-[2-methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-46		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide
Compound 1-47		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide

Table 1-7

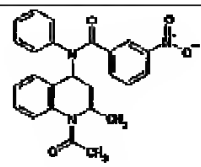
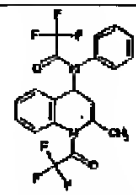
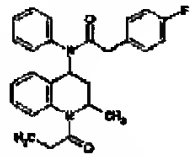
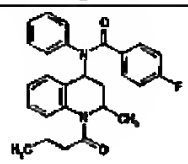
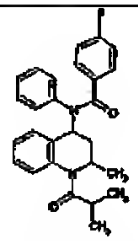
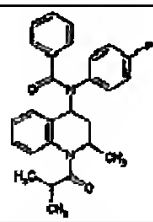
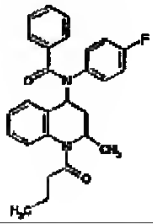
Compound 1-48		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-nitrobenzamide
Compound 1-49		N-(2-methyl-1-trifluoroacetyle-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyltrifluoroacetamide
Compound 1-50		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-pheynyl-4-fluorophenylacetamide
Compound 1-51		N-(1-butyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-fluorobenzamide
Compound 1-52		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-fluorobenzamide
Compound 1-53		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-(4-fluorophenyl)benzamide
Compound 1-54		N-(1-butyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(4-fluorophenyl)benzamide

Table 1-8

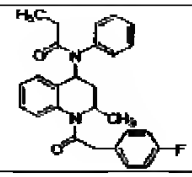
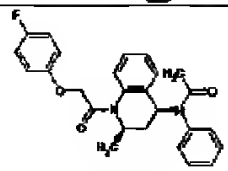
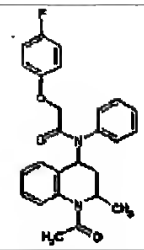
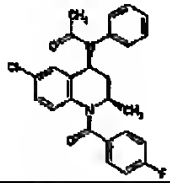
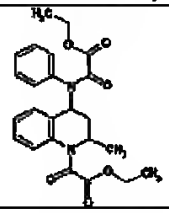
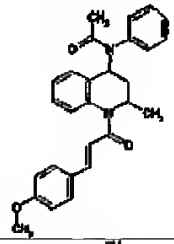
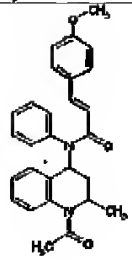
Compound 1-55		N-[1-(4-flurophenyl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpropionamide
Compound 1-56		N-[(2*S**, 4*R**)-1-(4-fluorophenoxy)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-57		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(4-flurophenoxy)acetamide
Compound 1-58		N-[(2*S**, 4*R**)-6-chloro-1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-59		N-(1- ethoxyoxalyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylethoxyoxalylamide
Compound 1-60		N-[1-(4-methoxycinnamoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-61		N-[1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methoxycinnamamide

Table 1-9

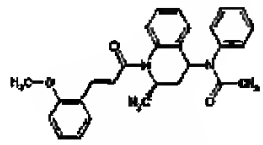
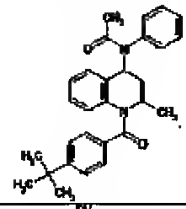
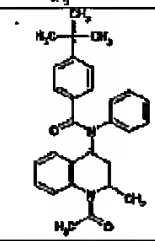
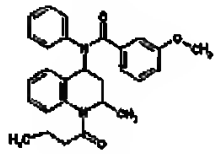
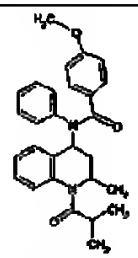
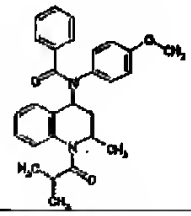
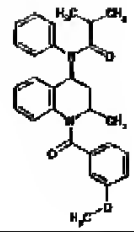
Compound 1-62		N-[(2*S**, 4*R**)-1-(2-methoxycinnamoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-63		N-[1-(4-tert-butylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-64		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-tert-butylbenzamide
Compound 1-65		N-(1-butyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-methoxybenzamide
Compound 1-66		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-methoxybenzamide
Compound 1-67		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-4-methoxyphenylbenzamide
Compound 1-68		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylisobutylamide

Table 1-10

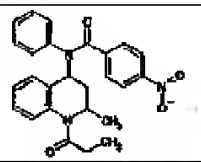
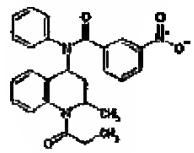
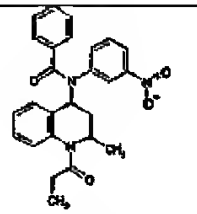
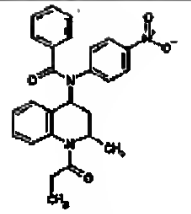
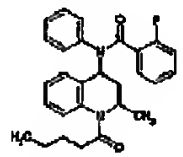
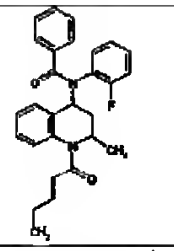
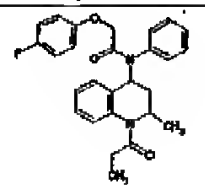
Compound 1-69		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-70		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-nitrobenzamide
Compound 1-71		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide
Compound 1-72		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(4-nitrophenyl)benzamide
Compound 1-73		N-(2-methyl-1-valeryl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-fluorobenzamide
Compound 1-74		N-(2-methyl-1-valeryl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(2-fluorophenyl)benzamide
Compound 1-75		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(4-fluorophenoxy)acetamide

Table 1-11

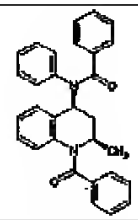
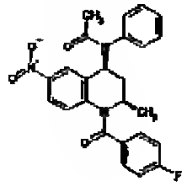
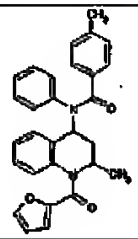
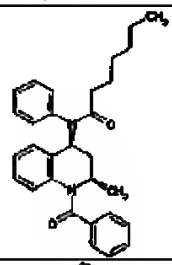
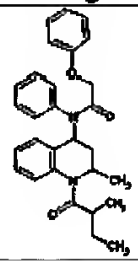
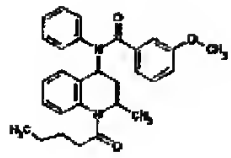
Compound 1-76		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylbenzamide
Compound 1-77		N-[(2*S**, 4*R**)-1-(4-fluorobenzoyl)-2-methyl-6-nitro-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-78		N-[1-(furan-2-carbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methylbenzamide
Compound 1-79		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylheptanamide
Compound 1-80		N-[1-(2-methylbutyryl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(phenoxy)acetamide
Compound 1-81		N-(2-methyl-1-valeryl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-methoxybenzamide

Table 1-12

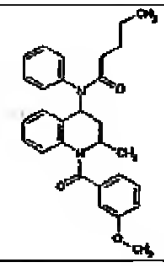
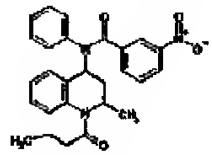
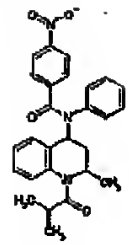
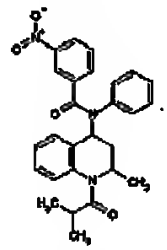
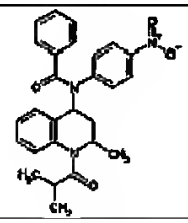
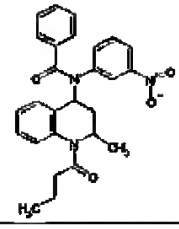
Compound 1-82		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylvaleramide
Compound 1-83		N-(1-butyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-nitrobenzamide
Compound 1-84		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-85		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-86		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide
Compound 1-87		N-(1-butyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide

Table 1-13

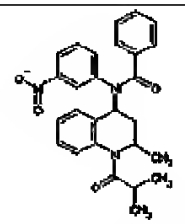
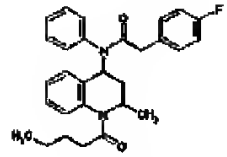
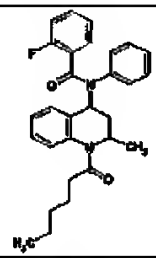
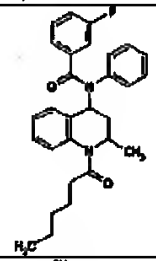
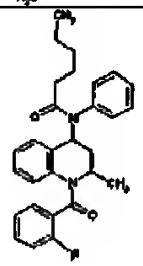
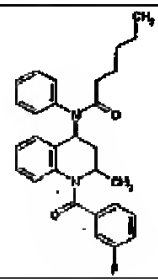
Compound 1-88		N-(1-isobutyryl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide
Compound 1-89		N-(2-methyl-1-valeryl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(4-fluorophenyl)acetamide
Compound 1-90		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-fluorobenzamide
Compound 1-91		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-fluorobenzamide
Compound 1-92		N-[1-(2-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylhexanamide
Compound 1-93		N-[1-(3-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylhexanamide

Table 1-14

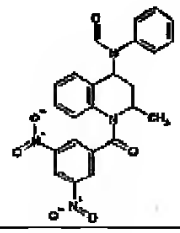
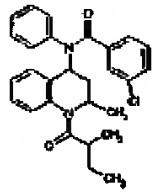
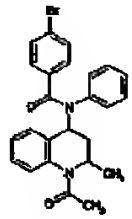
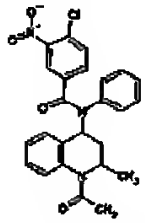
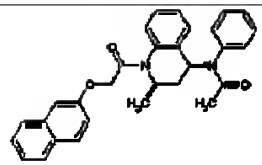
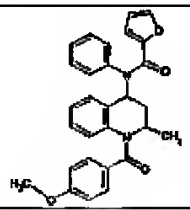
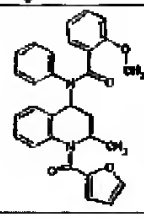
Compound 1-94		N-[1-(3,5-dinitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylformamide
Compound 1-95		N-[1-(2-methylbutyryl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-chlorobenzamide
Compound 1-96		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-bromobenzamide
Compound 1-97		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-chloro-3-nitrobenzamide
Compound 1-98		N-[(2*S**, 4*R**)-2-methyl-1-(naphthalene-2-yloxy)acetyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-99		N- [1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylfuran-2-carboxamide
Compound 1-100		N-[1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-methoxybenzamide

Table 1-15

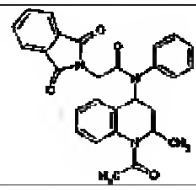
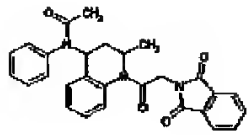
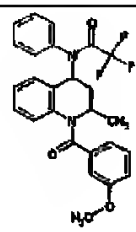
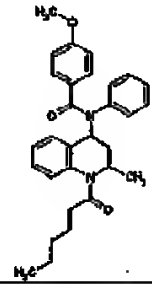
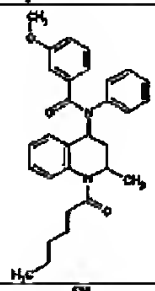
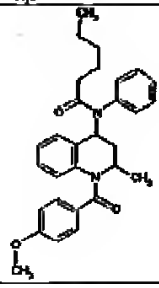
Compound 1-101		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(1,3-dioxo-1,3- dihydroxyindole-2-yl)acetamide
Compound 1-102		N-[1-(1,3-dioxyo-1,2-dihydroxyindole-2-yl)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-103		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyltrifluoroacetamide
Compound 1-104		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-methoxybenzamide
Compound 1-105		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-methoxybenzamide
Compound 1-106		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylhexanamide

Table 1-16

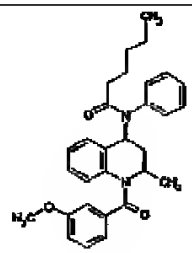
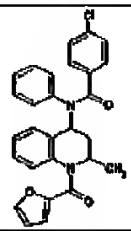
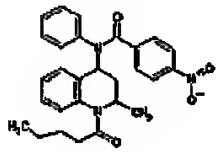
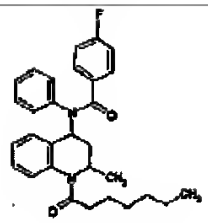
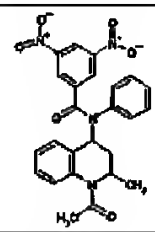
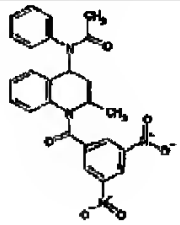
Compound 1-107		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylhexanamide
Compound 1-108		N-[1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-chlorobenzamide
Compound 1-109		N-(1-heptanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-110		N-(1-heptanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-fluorobenzamide
Compound 1-111		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3,5-dinitrobenzamide
Compound 1-112		N-[1-(3,5-dinitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide

Table 1-17

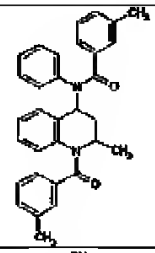
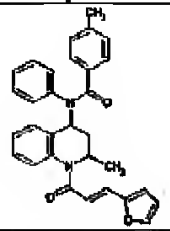
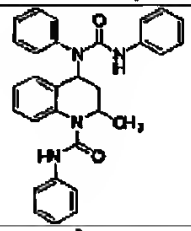
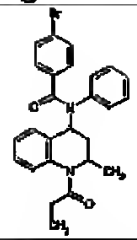
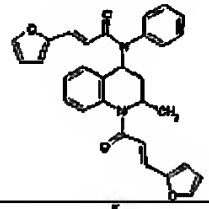
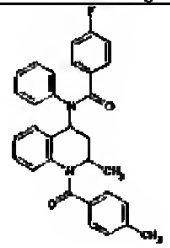
Compound 1-113		N-[1-(3-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-methylbenzamide
Compound 1-114		N-{1-[3-(2-furyl)acryloyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-4-methylbenzamide
Compound 1-115		N-[2-methyl-1-(N-phenylamino)carbonyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-N'-phenylurea
Compound 1-116		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-bromobenzamide
Compound 1-117		N-{1-[3-(2-furyl)acryloyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-3-(2-furyl)acryloamide
Compound 1-118		N-[1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-fluorobenzamide

Table 1-18

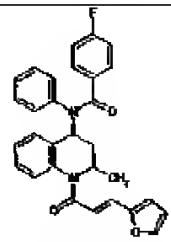
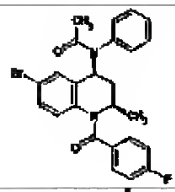
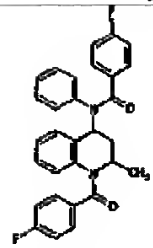
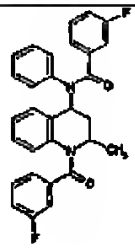
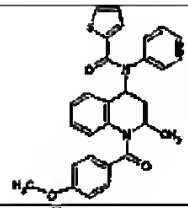
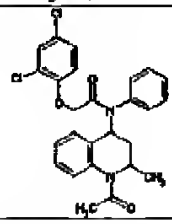
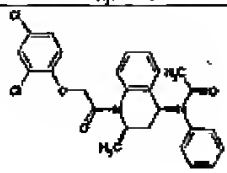
Compound 1-119		N-{1-[3-(2-furyl)acryloyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-4-fluorobenzamide
Compound 1-120		N-[(2*S**, 4*R**)-6-bromo-1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-121		N-[1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-fluorobenzamide
Compound 1-122		N-[1-(3-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-fluorobenzamide
Compound 1-123		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N- phenylthiophene-2-carboxamide
Compound 1-124		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(2,4-dichlorophenoxy)acetamide
Compound 1-125		N-{(2*S**, 4*R**)-1-[(2,4-dichlorophenoxy)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylacetamide

Table 1-19

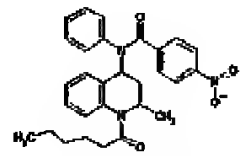
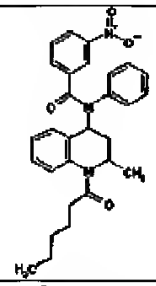
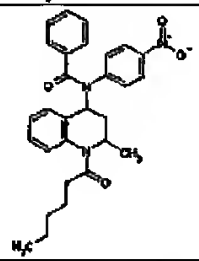
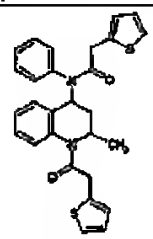
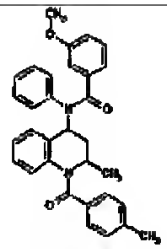
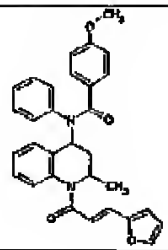
Compound 1-126		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-127		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-nitrobenzamide
Compound 1-128		N-(1-hexanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(4-nitrophenyl)benzamide
Compound 1-129		N-{1-[(2-thienyl)acetyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl(2-thienyl)acetamide
Compound 1-130		N-[1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-methoxybenzamide
Compound 1-131		N-{1-[3-(2-furyl)acryloyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-4-methoxybenzamide

Table 1-20

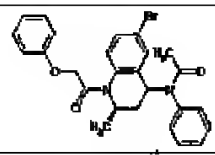
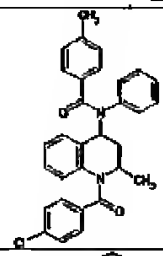
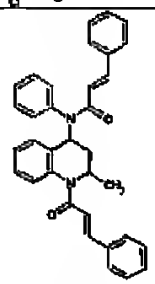
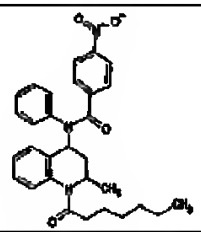
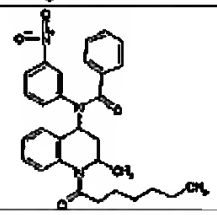
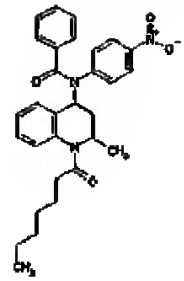
Compound 1-132		N-[(2*S**, 4*R**)-6-bromo-2-methyl-1-(2-phenoxyacetyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-133		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methylbenzamide
Compound 1-134		N-(1-cinnamoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylcinnamamide
Compound 1-135		N-(1-heptanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-136		N-(1-heptanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3-nitrophenyl)benzamide
Compound 1-137		N-(1-heptanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(4-nitrophenyl)benzamide

Table 1-21

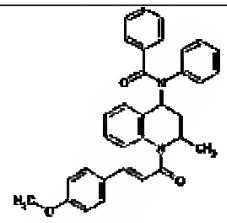
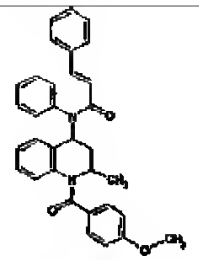
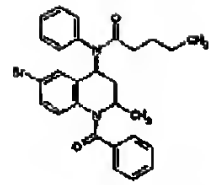
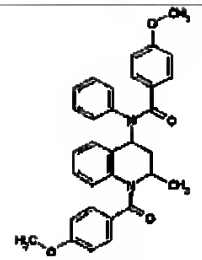
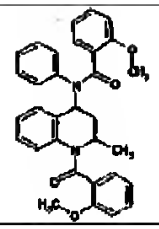
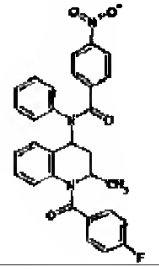
Compound 1-138		N-[1-(4-methoxycinnamoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylbenzamide
Compound 1-139		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcinnamamide
Compound 1-140		N-(1-benzoyl-6-bromo-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylpentanamide
Compound 1-141		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methoxybenzamide
Compound 1-142		N-[1-(2-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-methoxybenzamide
Compound 1-143		N-[1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-nitrobenzamide

Table 1-22

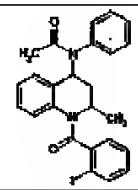
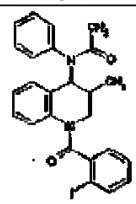
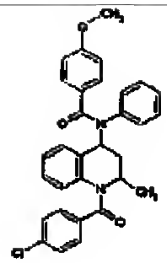
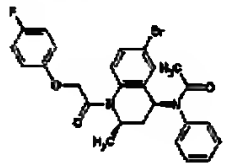
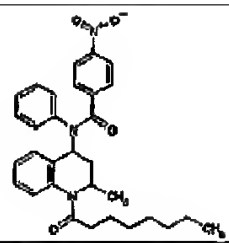
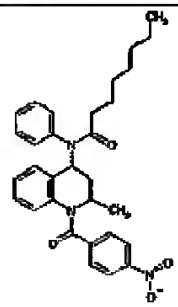
Compound 1-144		N-[1-(2-iodobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-145		N-[1-(2-iodobenzoyl)-3-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-146		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methoxybenzamide
Compound 1-147		N-[(2*S**, 4*R**)-6-bromo-1-(4-fluorophenoxy)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-148		N-(1-octanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-nitrobenzamide
Compound 1-149		N-[1-(4-nitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyloctanamide

Table 1-23

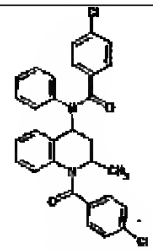
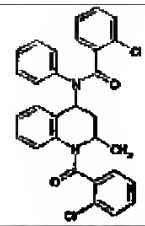
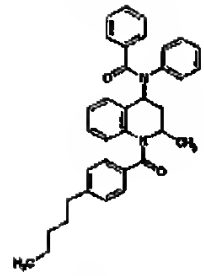
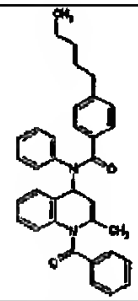
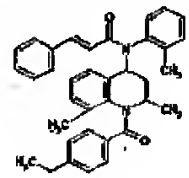
Compound 1-150		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-chlorobenzamide
Compound 1-151		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-chlorobenzamide
Compound 1-152		N-[1-(4-pentylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylbenzamide
Compound 1-153		N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-4-pentylbenzamide
Compound 1-154		N-[1-(4-ethylbenzoyl)-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-methylphenyl)-3-phenylacryloamide

Table 1-24

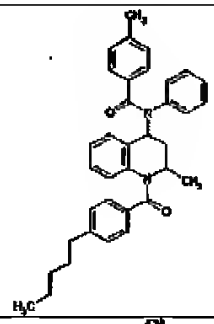
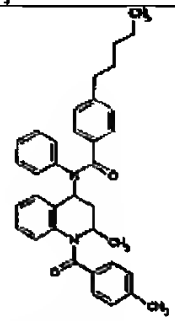
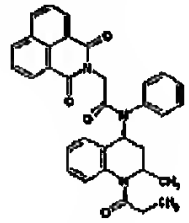
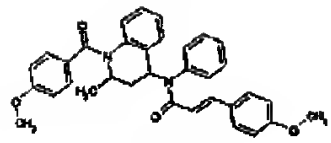
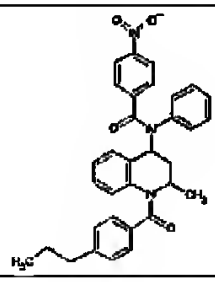
Compound 1-155		N-[1-(4-pentylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methylbenzamide
Compound 1-156		N-[1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-pentylbenzamide
Compound 1-157		N-(2-methyl-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide
Compound 1-158		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-(4-methoxyphenyl)acryloamide
Compound 1-159		N-[2-methyl-1-(4-propylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-nitrobenzamide

Table 1-25

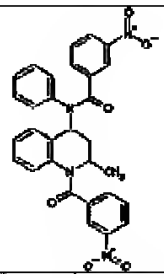
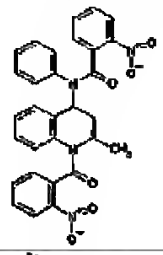
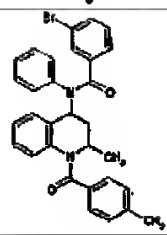
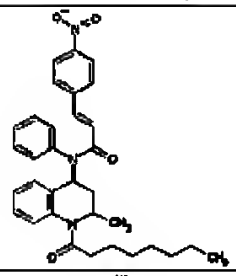
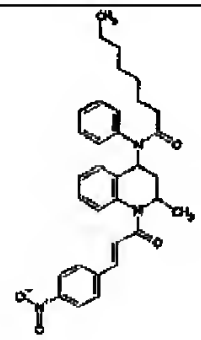
Compound 1-160		N-[1-(3-nitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-nitrobenzamide
Compound 1-161		N-[1-(2-nitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-nitrobenzamide
Compound 1-162		N-[1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-bromobenzamide
Compound 1-163		N-(1-octanoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-(4-nitrophenyl)acryloamide
Compound 1-164		N-[2-methyl-1-(4-nitrocinnamoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyloctanamide

Table 1-26

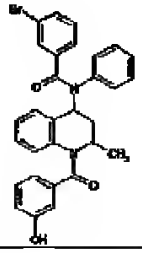
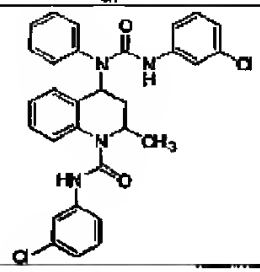
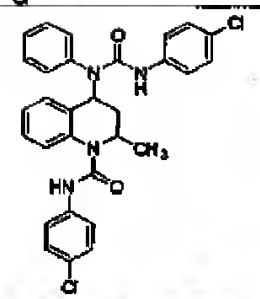
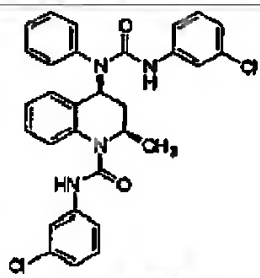
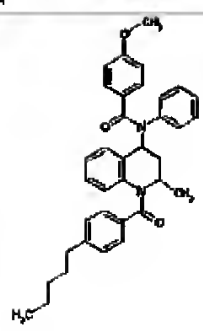
Compound 1-165		N-[1-(3-hydroxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-bromobenzamide
Compound 1-166		N-[1-(3-chlorophenylaminocarbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-N'-(3-chlorophenyl)urea
Compound 1-167		N-[1-(4-chlorophenylaminocarbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-N'-(4-chlorophenyl)urea
Compound 1-168		N-[(2*S**, 4*R**)-1-(3-chlorophenylaminocarbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-N'-(3-chlorophenyl)urea
Compound 1-169		N-[2-methyl-1-(4-pentylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methoxybenzamide

Table 1-27

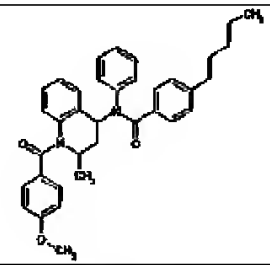
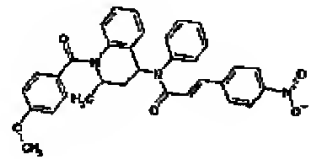
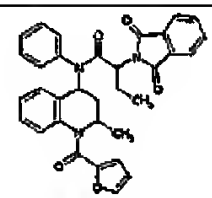
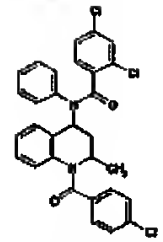
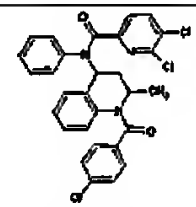
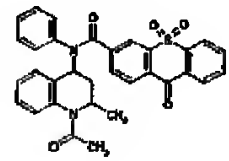
Compound 1-170		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-pentylbenzamide
Compound 1-171		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-nitrocinnamamide
Compound 1-172		N-[1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)butylamide
Compound 1-173		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2,4-dichlorobenzamide
Compound 1-174		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3,4-dichlorobenzamide
Compound 1-175		N-(1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-(9,10,10-trioxo-9,10-dihydro-10λ^6-thioxanthene-3-carboxamide

Table 1-28

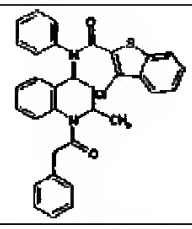
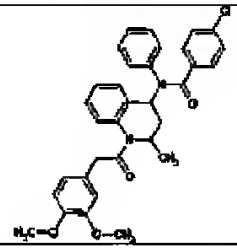
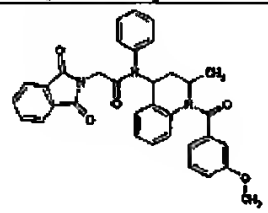
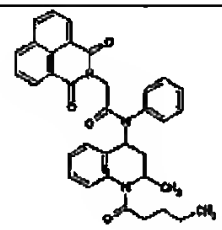
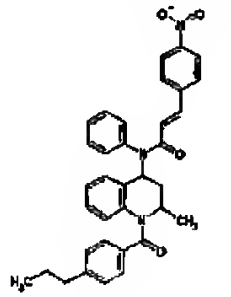
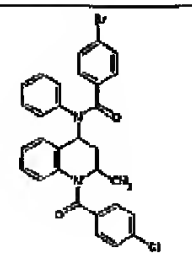
Compound 1-176		N-(1-phenylacetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-chlorobenzothiophene-2-carboxamide
Compound 1-177		N-[1-(3,4-dimethoxyphenyl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-chlorobenzamide
Compound 1-178		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(1,3-dioxy-1,3-dihydroisoindole-2-yl)acetamide
Compound 1-179		N-(2-methyl-1-pentanoyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide
Compound 1-180		N-[1-(4-propylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-nitrocinnamamide
Compound 1-181		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-bromobenzamide

Table 1-29

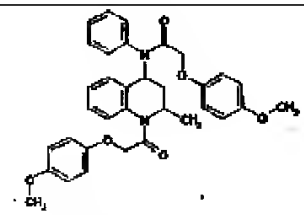
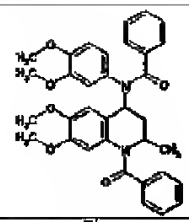
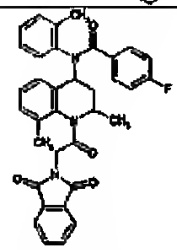
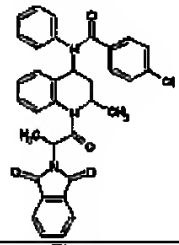
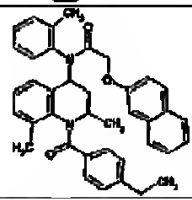
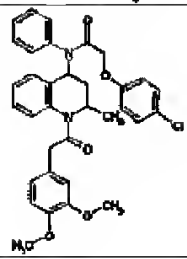
Compound 1-182		N-[1-(4-methoxyphenoxy)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(4-methoxyphenoxy)acetamide
Compound 1-183		N-(1-benzoyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-(3,4-dimethoxyphenyl)benzamide
Compound 1-184		N-[1-(1,3-dioxo-1,3-dihydroisoindole-2-yl)acetyl-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-methylphenyl)-4-fluorobenzamide
Compound 1-185		N-{1-[2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)propionyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-4-chlorobenzamide
Compound 1-186		N-[1-(4-ethylbenzoyl)-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-chlorophenyl)(naphthalene-2-yloxy)acetamide
Compound 1-187		N-[1-(3,4-dimethoxyphenyl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(4-chlorophenoxy)acetamide

Table 1-30

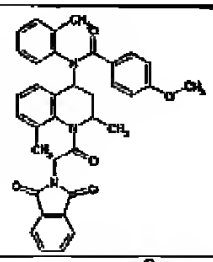
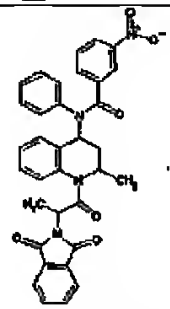
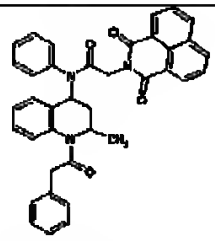
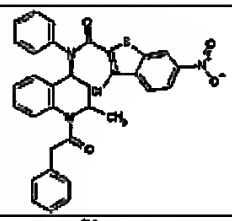
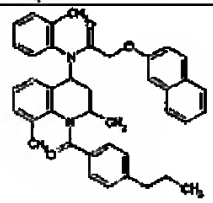
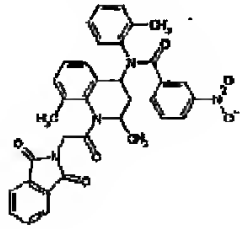
Compound 1-188		N-[1-(1,3-dioxo-1,3-dihydroisoindole-2-yl)acetyl-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-methylphenyl)-4-methoxybenzamide
Compound 1-189		N-{1-[2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)propionyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-3-nitrobenzamide
Compound 1-190		N-(2-methyl-1-phenylacetyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide
Compound 1-191		N-(1-phenylacetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-3-chloro-6-nitrobenzotheophene-2-carboxamide
Compound 1-192		N-[2,8-dimethyl-1-(4-propylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-methylphenyl)(naphthalene-2-yloxy)acetamide
Compound 1-193		N-[1-(1,3-dioxo-1,3-dihydroisoindole-2-yl)acetyl-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-methylphenyl)-3-nitrobenzamide

Table 1-31

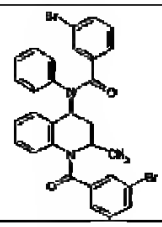
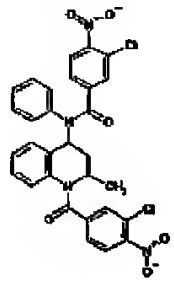
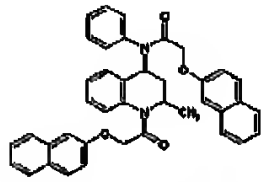
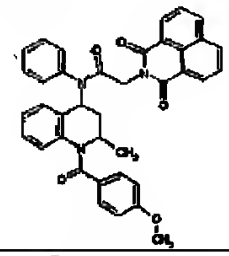
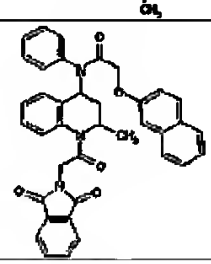
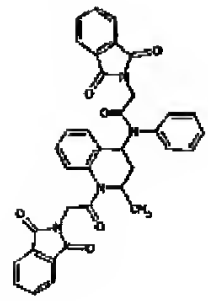
Compound 1-194		N-[1-(3-bromobenzoyl)- 2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-bromobenzamide
Compound 1-195		N-[1-(3-chloro-4-nitrobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-chloro-4-nitrobenzamide
Compound 1-196		N-[1-(naphthalene-2-yloxy)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(naphthalene-2-yloxy)acetamide
Compound 1-197		N-[1-(4-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide
Compound 1-198		N-[1-(1,3-dioxy-1,3-dihydroisoindole-2-yl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-(naphthalene-2-yloxy)acetamide
Compound 1-199		N-[1-(1,3-dioxo-1,3-dihydroisoindole-2-yl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(1,3-dioxo-1,3-dihydroisoindole-2-yl)acetamide

Table 1-32

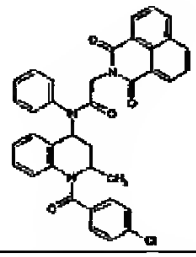
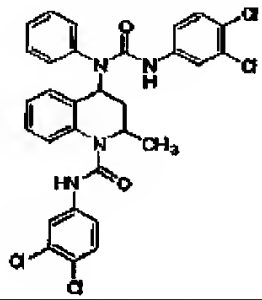
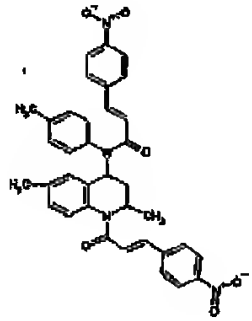
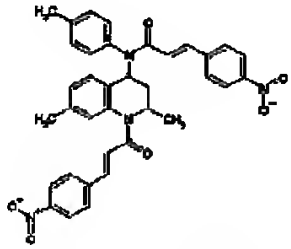
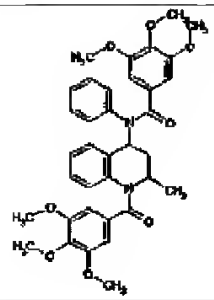
Compound 1-200		N-[1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide
Compound 1-201		N-[1-(3,4-dichlorophenylaminocarbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-N'-(3,4-dichlorophenyl)urea
Compound 1-202		N-[1-(4-nitrocinnamoyl)-2,6-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(4-methylphenyl)-4-nitrocinnamamide
Compound 1-203		N-[1-(4-nitrocinnamoyl)-2,7-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(4-methylphenyl)-4-nitrocinnamamide
Compound 1-204		N- [1-(3,4,5-trimethoxy)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3,4,5-trimethoxybenzamide

Table 1-33

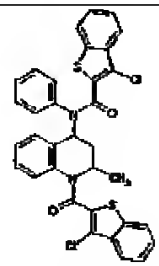
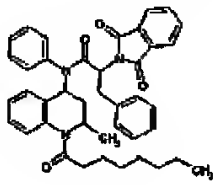
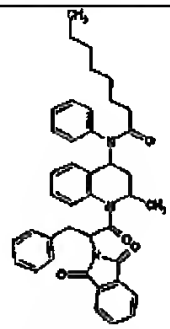
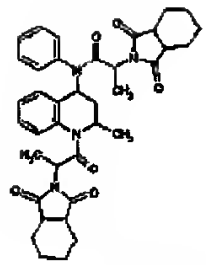
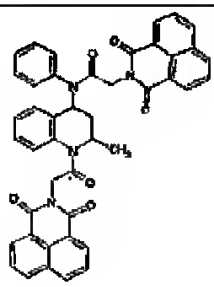
Compound 1-205		N-[1-(3-chlorobenzothiophene-2-carbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-chlorobenzothiophene-2-carboxamide
Compound 1-206		N-(2-methyl-1-octanoyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenyl-2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)-3-phenylpropionamide
Compound 1-207		N-{1-[2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)-3-phenylpropionyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyloctanamide
Compound 1-208		N-{1-[2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)propionyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenyl-2-(1,3-dioxo-1,3-dihydroisoindole-2-yl)propionamide
Compound 1-209		N-[1-(1,3-dioxo-1H,3H-benzo[de]isoquinoline-2-yl)acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl(1,3-dioxo-1H,3H-benzoisoquinoline-2-yl)acetamide

Table 1-34

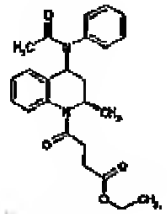
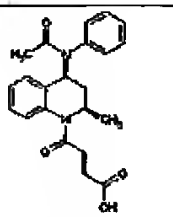
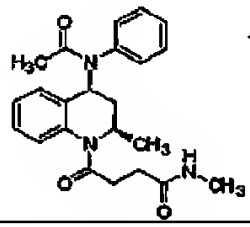
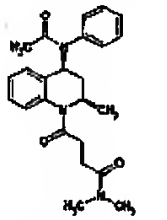
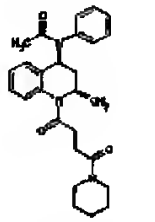
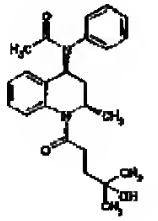
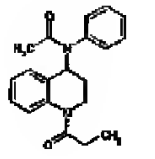
Compound 1-210		N-[(2*S**, 4*R**)-1-(4-ethoxycarbonylpropionyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-211		N-[(2*S**, 4*R**)-1-(4-carboxypropionyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-212		N-[(2*S**, 4*R**)-1-(N-acetyl-N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N'-methylbutanediamide
Compound 1-213		N-[(2*S**, 4*R**)-1-(N-acetyl-N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N',N'-dimethylbutanediamide
Compound 1-214		N-[(2*S**, 4*R**)-2-methyl-1-(4-oxo-4-piperidinobutyryl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-215		N-[(2*S**, 4*R**)-2-methyl-1-(4-hydroxy-4-methylvaleryl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-216		N-(1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylacetamide

Table 1-35

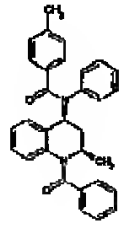
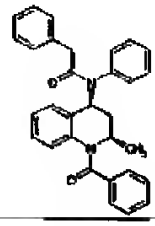
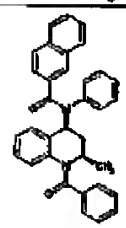
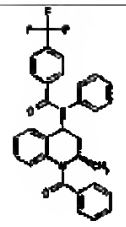
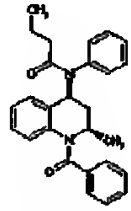
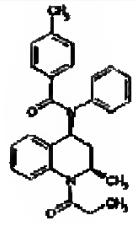
Compound 1-217		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methylbenzamide
Compound 1-218		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-phenylacetamide
Compound 1-219		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylnaphthalene-2-carboxamide
Compound 1-220		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-trifluoromethylbenzamide
Compound 1-221		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylbutylamide
Compound 1-222		N-[(2*S**, 4*R**)-1-propionyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-4-methylbenzamide

Table 1-36

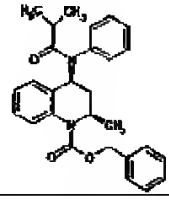
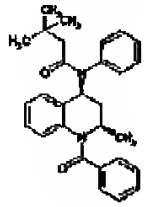
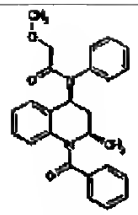
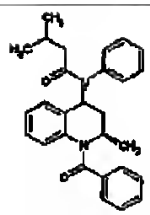
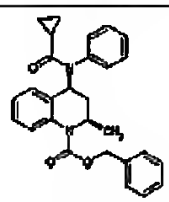
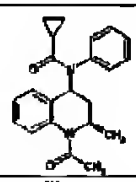
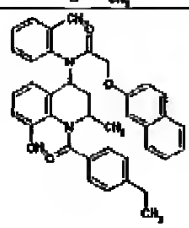
Compound 1-223		N-[(2*S**, 4*R**)-1-benzyloxycarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylisobutylamide
Compound 1-224		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3,3-dimethylvaleramide
Compound 1-225		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-methoxyacetamide
Compound 1-226		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-methylbutylamide
Compound 1-227		N-[(2*S**, 4*R**)-1-benzyloxycarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpropanecarboxamide
Compound 1-228		N-[(2*S**, 4*R**)-1-acetyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 1-229		N-[1-(4-ethylbenzoyl)-2,8-dimethyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(2-phenylmethyl)naphthalene-2-yloxyacetamide

Table 1-37

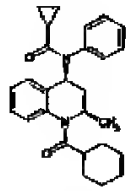
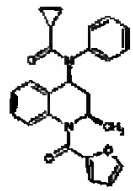
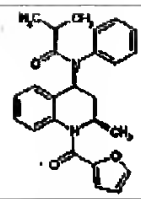
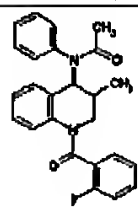
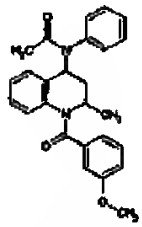
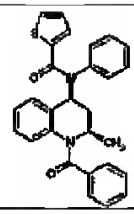
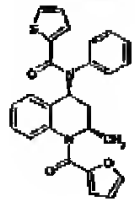
Compound 1-230		N-[(2*S**, 4*R**)-1-(cyclohexanecarbonyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 1-231		N-[(2*S**, 4*R**)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 1-232		N-[(2*S**, 4*R**)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-methylpropionamide
Compound 1-233		N-[1-(2-iodobenzoyl)-3-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-234		N-[1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 1-235		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylthiophene-2-carboxamide
Compound 1-236		N-[(2*S**, 4*R**)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylthiophene-2-carboxamide

Table 1-38

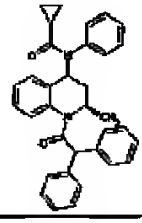
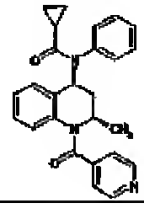
Compound 1-237		N-[(2*S**, 4*R**)-1-(diphenylacetyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 1-238		N-[(2*S**, 4*R**)-1-isonicotinoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide

Table 2

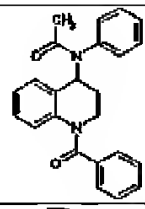
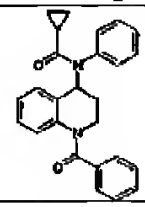
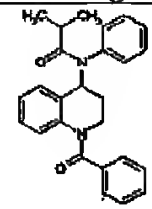
Compound 2-1		N-[1-benzoyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide
Compound 2-2		N-[1-benzoyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 2-3		N-[1-benzoyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylisobutyrylamide

Table 3-1

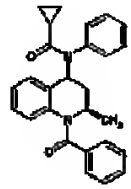
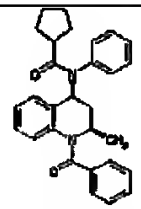
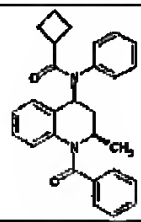
Compound 3-1		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-2		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopentanecarboxamide
Compound 3-3		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclobutanecarboxamide

Table 3-2

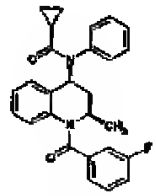
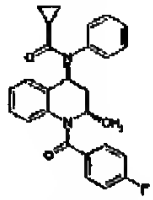
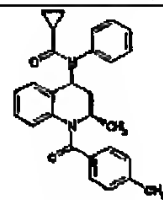
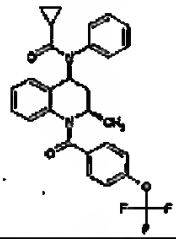
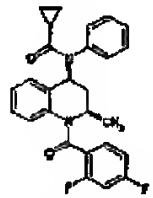
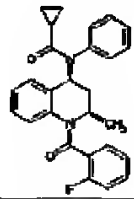
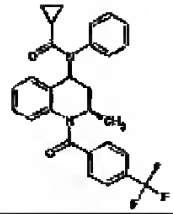
Compound 3-4		N-[(2*S**, 4*R**)-1-(3-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-5		N-[(2*S**, 4*R**)-1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-6		N-[(2*S**, 4*R**)-1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-7		N-[(2*S**, 4*R**)-1-(4-trifluoromethoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-8		N-[(2*S**, 4*R**)-1-(2,4-difluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-9		N-[(2*S**, 4*R**)-1-(2-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-10		N-[(2*S**, 4*R**)-1-(4-trifluoromethylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide

Table 3-3

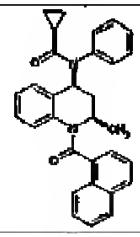
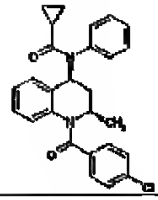
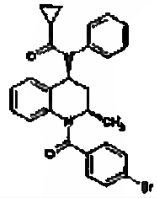
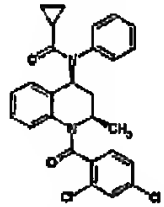
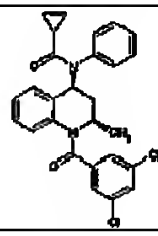
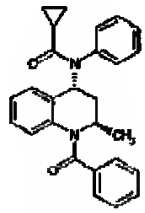
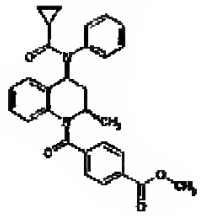
Compound 3-11		N-[(2*S**, 4*R**)-1-(1-naphthoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-12		N-[(2*S**, 4*R**)-1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-13		N-[(2*S**, 4*R**)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-14		N-[(2*S**, 4*R**)-1-(2,4-dichlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-15		N-[(2*S**, 4*R**)-1-(3,5-dichlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-16		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-17		N-[(2*S**, 4*R**)-1-(4-methoxycarbonylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide

Table 3-4

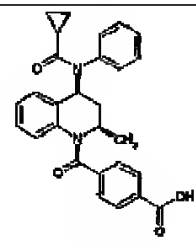
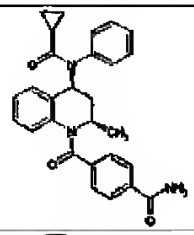
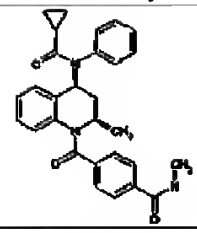
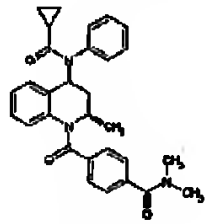
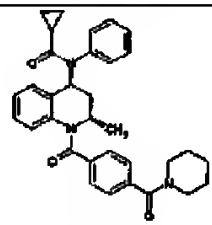
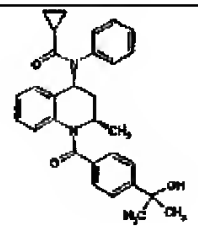
Compound 3-18		N-[(2*S**, 4*R**)-1-(4-carboxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-19		N-[(2*S**, 4*R**)-1-(4-aminocarbonylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-20		N-{(2*S**, 4*R**)-2-methyl-1-[4-(N-methylaminocarbonyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide
Compound 3-21		N-{(2*S**, 4*R**)-1-[4-(N, N-dimethylaminocarbonyl)benzoyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide
Compound 3-22		N-{(2*S**, 4*R**)-1-[4-(piperidinocarbonyl)benzoyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide
Compound 3-23		N-{(2*S**, 4*R**)-1-[4-(2-hydroxy-2-methylethyl)benzoyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide

Table 3-5

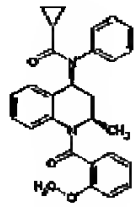
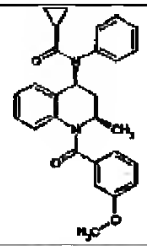
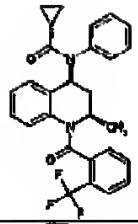
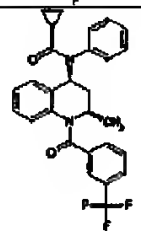
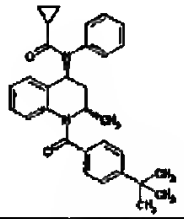
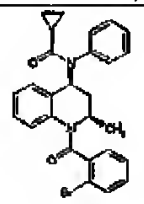
Compound 3-24		N-[(2*S**, 4*R**)-1-(2-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-25		N-[(2*S**, 4*R**)-1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-26		N-[(2*S**, 4*R**)-2-methyl-1-(2-trifluoromethoxybenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-27		N-[(2*S**, 4*R**)-2-methyl-1-(3-trifluoromethoxybenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-28		N-[(2*S**, 4*R**)-1-[4-(tert-butyl)benzoyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-29		N-[(2*S**, 4*R**)-1-(2-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide

Table 3-6

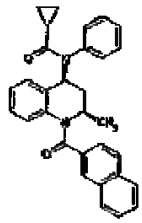
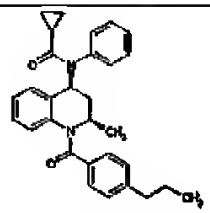
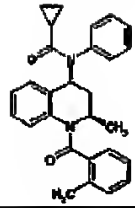
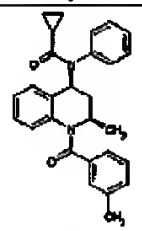
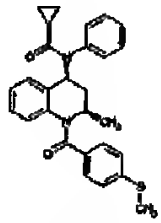
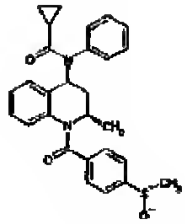
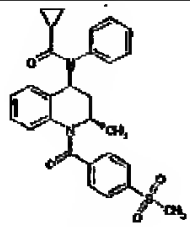
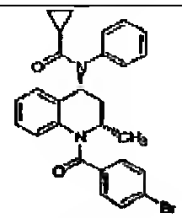
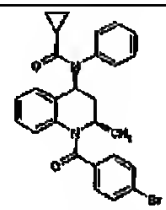
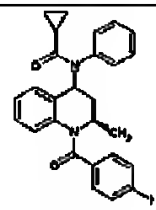
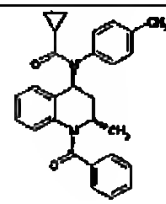
Compound 3-30		N- N-[(2*S**, 4*R**)-2-methyl-1-(2-naphthoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-31		N-[(2*S**, 4*R**)-2-methyl-1-(4-propylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-32		N-[(2*S**, 4*R**)-2-methyl-1-(2-methylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-33		N-[(2*S**, 4*R**)-2-methyl-1-(3-methylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-34		N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylthio)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide
Compound 3-35		N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylsulfinyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide

Table 3-7

Compound 3-36		N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylsulphonyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide
Compound 3-37		N-[(2*S*, 4*R*)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-38		N-[(2*R*, 4*S*)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-39		N-[(2*S**, 4*R**)-1-(4-iodobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide
Compound 3-40		N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-(4-methylphenyl)cyclopropanecarboxamide

The administration route of the medicine of the present invention is not limited in particular, and the most effective route of administration can be selected accordingly from an oral or a non-oral administration. Examples of drug formulation that is appropriate for oral administration include tablet, granules, capsules and the like. Examples of preparation that is appropriate for non-oral administration include injection and the like. Commonly known method is employed to formulate the dosage forms utilized for the abovementioned oral or non-oral administration, and each formulation may contain various types of diluent, binder, disintegrating agent, surfactant, suspending agent, tonicity agent, emulsifier, and the like.

Examples of diluent, as carriers of formulation, include sucrose, lactose, mannitol, glucose, microcrystalline cellulose, and the like; examples of binder include hydroxypropylcellulose, and the like; examples of disintegrating agent include starch, alginic acid, polyvinylpyrrolidone, and the like; examples of surfactant include magnesium stearate, talc, and the like; examples of suspending agent include propylene glycol, calcium hydrogen phosphate, and the like; tonicity agent include sodium citrate, and the like; examples of emulsifier include ethanol, sorbitan fatty acid ester, and the like.

The amount and frequency of dosage of Compound (I), (II), (III), and pharmacologically acceptable salts of the compounds are not limited in particular, and preferably, adjusted according to the various types of factors, such as the type of disease, severity, form of administration, patient's age and weight, presence of complications, and the like.

Pharmacological properties of typical compound (I), (II), and (III) are illustrated in detail in the following examples of test:

TEST 1: Inhibitive effect on antigen-induced cell infiltration

Male Balb/c mice (Charles River Japan) were sensitized by intraperitoneal injections of saline suspension containing an antigen, egg white albumin (50 μg), and aluminum hydroxide (1 mg) twice, seven days apart. Two weeks after the last sensitization to mice, saline solution of 1 % egg white albumin was administered by inhalation for 30 minutes. Similarly, an antigen was administered by inhalation again in four and eight days: a total of three antigen inhalation inductions were performed. Sham-induced group of mice received a total of three inhalations of saline solution in the same manner as the antigen-induced group of mice. About 24 hours after the last inhalation, an alveolar wash was performed by injecting 1 ml of *Hanks' balanced salt solution* (*Invitrogen Co.*) from cannula, which was installed in the respiratory tract of mice, and then the wash fluid was collected. The number of cells included in the collected alveolar wash fluid was counted using a cell counter. Then, smears were prepared, dyed with Diff-Quick, and the

cell composition was studied. The number of eosinophils was calculated by multiplying the ratio of eosinophils contained in the total cell and the total cell count. Test compounds were suspended in 0.5 % methylcellulose solution, adjusting the concentration to 30 mg/ kg or 100 mg/ kg, and orally administered for nine days from the date of the first antigen inhalation until the date of the final inhalation. The test compounds were administered one hour prior to the antigen inhalation on the day of inhalation. Each group contained eight mice.

The number of eosinophils in alveolar wash fluids of the contrast group (solvent (0.5 % methyl cellulose solution)-administered group) was $(1.8 \pm 0.2) \times 10^5$ (average ± standard error) per subject. A significant decrease in the number of eosinophils in alveolar wash fluids, however, was observed in the group that received administration of 30 mg of Compound 1-20 (19.7 % decrease) and 100 mg of Compound 1-20 (48.6 % decrease).

TEST 2: Inhibitive effect on eosinophil chemotaxis

The red blood cells in the peripheral blood (including 1/10 volume of 3.8 % sodium citrate) of healthy human subject were removed by precipitation using Dextran T-500 (Amersham Pharmacia Biotech) to collect the supernatant including the white blood cells. The granulocyte fraction comprising neutrophils and eosinophils was then isolated from the white blood cells by discontinuous density-gradient centrifugation using Ficoll-Paque™ PLUS (Amersham Pharmacia Biotech). A small number of red blood cells contained in the granulocyte fraction were removed by hemolysis. The collected granulocyte fraction was rinsed with bovine serum albumin in phosphate-buffered saline (BSA/PBS) containing 0.2 % bovine serum albumin (BSA), and then suspended in the BSA/PBS. After adjusting the number of cells to 1×10^9/ ml, anti-CD16-coated magnetic beads (Miltenyi Biotec) were conjugated with neutrophils, and the neutrophils were removed using LD Columns (Miltenyi Biotec) and a magnetic cell separator (Miltenyi Biotec) to isolate the eosinophils. The isolated eosinophils were suspended in RPMI medium (FBS-RPMI) containing10 % fetal calf serum (Intergen), and adjusted to 1×10^6 cells/ ml. Using the pore size 3 μm, 24-well Micro Chemotaxis Transwell™ plate (Croning Incorporated), the influence of the test compounds on the eosinophil chemotaxis stimulated by prostaglandin D_2 (PGD_2) (Cayman Chemical) was studied. 500 μl of FBS-RPMI solution containing 100 nmol/l of PGD_2 and 10 μmol/l of a test compound was poured into the bottom chamber plate, and heated to 37 degrees Celsius. For the test compounds, 10 nmol/l dimethylsulfoxide (DMSO) solution was prepared, and added to the solution in the bottom plate until the final DMSO concentration reached 0.1 %. 100 μl of eosinophil suspension (1×10^6 cells/ ml) heated to 37 degrees Celsius was poured into the top cup, and incubated for three hours at 37

degrees Celsius and 5 % carbon dioxide. After completion of incubation, the top cup was removed, and the fluid in the bottom chamber that contains migrated cells was collected. Fluorosphere suspension (FlowCount™, Beckman Coulter) with a set number of particles was added to the collected fluid, and the number of eosinophils contained in the collected fluid was counted by a flow cytometer. The number of fluorospheres was subtracted from the cell count to obtain the final number of eosinophils in 500 µl. Table 4 shows the rate of chemotaxis inhibited by the test compounds:

TABLE 4

Test Compounds	Chemotaxis inhibition rate
Compound 1-4	93 %
Compound 1-7	71%
Compound 1-8	86%
Compound 1-11	95%
Compound 1-18	67%
Compound 1-20	98%
Compound 1-24	8%
Compound 1-63	92%
Compound 1-133	74%
Compound 1-166	28%
Compound 1-217	83%
Compound 1-221	92%
Compound 1-223	82%
Compound 1-225	92%
Compound 3-1	91%
Compound 3-3	82%

TEST 3: Acute toxicity test

Test compounds were orally administered to male dd mice (weight: 20 ± 1 g (n = 3)). As a result, the minimum lethal dose (MLD) of Compound 3-1 was less than 100 mg/ kg (mice, oral), which confirmed the safety of the compounds of present invention.

The best examples to implement the invention

The following Examples and References are provided to further illustrate the present invention in detail, but not limit the scope of the present invention. The number of compounds used in Examples and References corresponds to the number of Compounds in Table 1-1 through 1-38, Table 2, as well as Table 3-1 through 3-7.

EXAMPLE 1

N-[(2*S**, 4*R**)-1-(4-ethoxycarbonylpropionyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide (Compound 1-210)

Methylene chloride (10 ml) solution of (2*S**, 4*R**)-4-(N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline (Canadian Journal of Chemistry (Can. J. Chem.), vol. 42, p. 2885 (1969)) (1.9 g) and pyridine (10 ml) was cooled to 0 degrees Celsius, and monoethylsuccinate chloride (1.7 ml) was added slowly while stirring the mixture. After stirring for 30 minutes at the same temperature, saturated sodium hydrogen carbonate solution was added, and the mixture was eluted with chloroform. The solvent was distilled to obtain pale yellow liquid (1.61 g), and the liquid was dissolved in tetrahydrofuran (100 ml). Sodium hydride (351 mg) was added to the liquid and stirred for 30 minutes at room temperature. The mixture was cooled to -78 degrees Celsius, acetyl chloride (627 µl) was added, and stirred for 12 hours at room temperature. Water was added to the reaction mixture, and the solvent was distilled after eluted with chloroform. Pyridine (20 ml) and methylene chloride (20 ml) were added to the distillation residue, and acetyl chloride (351 µl) was added slowly at 0 degrees Celsius. After stirring for 2 hours at room temperature, saturated sodium hydrogen carbonate solution was added. The mixture was eluted with chloroform, and the organic solvent was distilled under a reduced pressure. Compound 1-210 (1.69 g, 94 %) was obtained by refining the distillation residue using silica gel column chromatography (hexane:ethyl acetate = 2:1 followed by hexane:ethyl acetate = 1:2).

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 1.03 (d, J = 6.2 Hz, 3H), 1.23 (t, J = 7.3 Hz, 3H), 1.99 (s, 3H), 2.18 (br s, 1H), 2.39-2.95 (m, 5H), 4.11 (q, J = 7.3 Hz, 2H), 7.67-4.75 (m, 1H), 5.30 (br s, 1H), 7.21-7.38 (m, 9H).

ESIMS *m/z*: $[M+H]^+$ 409.

EXAMPLE 2

N-[(2*S**, 4*R**)-1-propionyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylacetamide (Compound 1-216)

p-toluenesulphonate (10 mg), aniline (0.18 ml) and toluene (50 ml) were added to 1-propionyl-2,3-dihydroquinoline-4-ones (EP243982) (200 mg), and heat refluxed for 12 hours. After left standing to cool down to room temperature, the solvent was distilled under a reduced pressure. Methanol (20 ml) and sodium borohydride (0.5 g) were added, and the mixture was stirred for 12 hours at room temperature. After adding saturated sodium hydrogen carbonate solution, the solvent was distilled under a reduced pressure and eluted with ethyl acetate. The solvent was distilled under a reduced pressure, and methylene

chloride (1 ml) and pyridine (1 ml) were added to the residue. Acetyl chloride (1 ml) was added at 0 degrees Celsius, and the mixture was stirred for 30 minutes at the same temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture, the mixture was eluted with chloroform, and the solvent was distilled under a reduced pressure. Compound 1-216 (44 g) was obtained by refining the distillation residue using preparative thin layer chromatography (hexane:ethyl acetate = 1:1).

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.94 (s, 3H), 1.88 (s, 3H), 1.90-2.09 (m, 2H), 2.15-2.38 (m, 3H), 3.33-3.43 (m, 1H), 3.90 (br s, 1H), 6.26 (t, J = 8.1 Hz, 1H), 6.87 (br s, 1H), 7.11-7.31 (m, 6H), 7.51-7.54 (m, 1H).

ESIMS *m/z*: $[M+H]^+$ 323.

EXAMPLE 3

N-[(2*S**, 4*R**)-1-benzyloxycarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylisobutylamide (Compound 1-223)

Under a dry nitrogen atmosphere, methylene chloride (6 ml) solution of (2*S**, 4*R**)-4-(N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline (Canadian Journal of Chemistry (Can. J. Chem.), vol. 42, p. 2885 (1969)) (1.1 g) and pyridine (6 ml) was prepared and cooled to 0 degrees Celsius. At 0 degrees Celsius, benzyl chloroformate (0.87 ml) was added to the solution, and the mixture was stirred for one hour at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture. The mixture was eluted with chloroform, and washed with hydrochloride (1 mol/l). 1,8-diazabicyclo[5.4.0]undec-7-ene (2.4 ml), dioxane (30 ml) and isobutyl chloride (5.9 ml) were added to the pale yellow oily matter obtained, and the mixture was stirred for 2 hours at 110 degrees Celsius. After distilling the solvent under a reduced pressure, methanol (100 ml) was added to the reaction mixture, and the solvent was distilled under a reduced pressure. Saturated sodium hydrogen carbonate solution was added to the mixture, and the mixture was eluted with ethyl acetate. The organic layer was washed with hydrochloride (1 mol/l, 100 ml). After solvent in the organic layer was distilled under a reduced pressure, the residue was recrystallized with hexane-ethyl acetate, and Compound 1-223 (1.38 g) was obtained as a colorless crystal.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.10 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.6 Hz, 6H), 1.52-1.61 (m, 1H), 2.17 (br s, 1H), 2.59 (sept, J = 6.6 Hz, 1H), 4.41-4.49 (m, 1H), 5.11 (d, J = 12.6 Hz, 1H), 5.25 (d, J = 12.6 Hz, 1H), 5.65 (br s, 1H), 7.14-7.43 (m, 14H).

ESIMS *m/z*: $[M+H]^+$ 443.

EXAMPLE 4

N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3,3-dimethylvaleramide (Compound 1-224)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 1 was reacted with tert-butylacetyl chloride to created Compound 1-224.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.06 (s, 9H), 1.15 (d, J = 6.3 Hz, 3H), 1.51-1.61 (m, 1H), 2.16 (s, 2H), 2.32 (br s, 1H), 4.74-4.82 (m, 1H), 5.65 (br s, 1H), 6.47 (dd, J = 0.9 Hz, 7.8 Hz, 1H), 6.87 (t, J = 7.5 Hz, 1H), 7.12-7.39 (m, 12H).

ESIMS *m/z*: $[M+H]^+$ 441.

EXAMPLE 5

N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-3-methylbutylamide (Compound 1-226)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 1 was reacted with isovaleryl chloride to created Compound 1-226.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.94 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.5 Hz, 3H), 1.15 (d, J = 6.2 Hz, 3H), 1.54-1.62 (m, 1H), 2.01-2.14 (m, 2H), 2.17-2.32 (m, 2H), 4.73-4.86 (m, 1H), 5.65 (br s, 1H), 6.49 (dd, J = 0.8, 7.8 Hz, 1H), 6.88 (t, J = 7.4 Hz, 1H), 7.12-7.40 (m, 12H).

ESIMS *m/z*: $[M+H]^+$ 427.

EXAMPLE 6

N-[(2*S**, 4*R**)-1-benzyloxycarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpropanecarboxamide (Compound 1-227)

Under a dry nitrogen atmosphere, methylene chloride (25 ml) solution of (2*S**, 4*R**)-4-(N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline (Canadian Journal of Chemistry (Can. J. Chem.), vol. 42, p. 2885 (1969)) (5.0 g) and pyridine (25 ml) was prepared and cooled to 0 degrees Celsius. At 0 degrees Celsius, benzyl chloroformate (3.26 ml) was added to the solution, and the mixture was stirred for one hour at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction

mixture. The mixture was eluted with ethyl acetate, and washed with hydrochloride (1 mol/l). 1,8-diazabicyclo[5.4.0]undec-7-ene (14 ml), dioxane (150 ml) and cyclopropanecarbonyl chloride (16 ml) were added to the pale yellow oily matter obtained, and the mixture was stirred for 24 hours at room temperature, and four hours at 90 degrees Celsius, and again for 12 hours at room temperature. After distilling the solvent under a reduced pressure, pyridine (25 ml), methylene chloride (25 ml) and cyclopropanecarbonyl chloride (5 ml) was added, and the mixture was stirred for 12 hours at room temperature. Methanol (100 ml) was added to the reaction mixture, and the solvent was distilled under a reduced pressure. Saturated sodium hydrogen carbonate solution was added to the mixture, and the mixture was eluted with ethyl acetate. The organic layer was washed with hydrochloride (1 mol/l, 100 ml). After solvent in the organic layer was distilled under a reduced pressure, the residue was refined with silica gel column chromatography (hexane:ethyl acetate:chloroform = 45:45:10), and Compound 1-227 (7.58 g, 82 %) was obtained as a colorless crystal.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.67-0.74 (m, 2H), 1.04-1.30 (m, 3H), 1.12 (d, J = 6.3 Hz, 3H), 1.38-1.46 (m, 1H), 2.15 (br s, 1H), 4.39-4.51 (m, 1H), 5.10 (d, J = 12.3 Hz, 1H), 5.25 (d, J = 12.3 Hz, 1H), 5.48 (br s, 1H), 7.16-7.44 (m, 14H).

ESIMS *m/z*: $[M+H]^+$ 441.

EXAMPLE 7

N-[(2*S**, 4*R**)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 1-231)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 3 was reacted with cyclopropanecarbonyl chloride to created Compound 1-231.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.66-0.73 (m, 2H), 1.06-1.18 (m, 3H), 1.15 (d, J = 6.0 Hz, 3H), 1.40-1.49 (m, 1H), 2.30 (br s, 1H), 4.65-4.74 (m, 1H), 5.52 (br s, 1H), 6.20-6.24 (m, 2H), 6.85 (d, J = 7.8 Hz, 1H), 7.10 (t, J = 7.7 Hz, 1H), 7.15-7.58 (m, 8H).

ESIMS *m/z*: $[M+H]^+$ 401.

EXAMPLE 8

N-[(2*S**, 4*R**)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenyl-2-methylpropionamide (Compound 1-232)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 3 was reacted with isobutyl chloride to created Compound 1-232.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 1.10 (br s, 1H), 1.13 (d, J = 6 Hz, 3H), 1.14 (d, J = 6.6 Hz, 3H), 1.16 (d, J = 6.6 Hz, 3H), 2.27 (br s, 1H), 2.62 (sept, J = 6.6 Hz, 1H), 4.66-4.73 (m, 1H), 5.47 (br s, 1H), 6.19-6.24 (m, 2H), 6.85 (d, J = 7.5 Hz, 1H), 7.10 (t, J = 7.7 Hz, 1H), 7.26-7.46 (m, 8H).

ESIMS *m/z*: $[M+H]^+$ 403.

EXAMPLE 9

N-[(2*S**, 4*R**)-1-isonicotinoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 1-238)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with isonicotinoyl to created Compound 1-238.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.73-0.77 (m, 2H), 1.05-1.19 (m, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.43-1.51 (m, 1H), 2.31 (br s, 1H), 4.73-4.85 (m, 1H), 5.65 (br s, 1H), 6.46 (d, J = 7.8 Hz, 1H), 6.92 (t, J = 7.5 Hz, 1H), 7.06 (dd, J = 4.5 Hz, 1.5 Hz, 2H), 7.23 (td, J = 7.2, 1.2 Hz, 1H), 7.37-7.42 (m, 6H), 8.48 (dd, J = 4.5, 1.5 Hz, 2H).

ESIMS *m/z*: $[M+H]^+$ 441.

EXAMPLE 10

N-(1-benzoyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylacetamide (Compound 2-1)

The compound, 4-(N-phenylamino)-1-benzoyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 4 was reacted with acetyl chloride to created Compound 2-1.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 1.92 (s, 3H), 2.04-2.17 (m, 1H), 2.26-2.35 (m, 1H), 3.45-3.55 (m, 1H), 4.16-4.24 (m, 1H), 6.40 (t, J = 8.6 Hz, 1H), 6.49 (d, J = 8.1 Hz, 1H), 6.86 (t, J = 7.1 Hz, 1H), 6.95-7.37 (m, 11H), 7.52 (d, J = 7.7 Hz, 1H).

ESIMS *m/z*: $[M+H]^+$ 371.

EXAMPLE 11

N-(1-benzoyl-1,2,3,4-tetrahydroquinoline-4-yl)-N-phenylisobutyrylamide (Compound 2-3)

The compound, 4-(N-phenylamino)-1-benzoyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 4 was reacted with isobutyryl chloride to created Compound 2-3.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 1.10 (d, J = 6.6 Hz, 3H), 1.12 (d, J = 6.6 Hz, 3H), 2.01-2.06 (m, 1H), 2.26-2.31 (m, 1H), 2.44 (sept, J = 6.6 Hz, 1H), 3.48-3.58 (m, 1H), 4.05-4.16 (m, 1H), 6.43 (t, J = 8.7 Hz, 1H), 6.50 (d, J = 8.1 Hz, 1H), 6.87 (t, J = 7.1 Hz, 1H), 6.96-7.47 (m, 12H).

ESIMS *m/z*: $[M+H]^+$ 399.

EXAMPLE 12

N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-1)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 1 was reacted with cyclopropanecarbonyl chloride to created Compound 3-1.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.67-0.76 (m, 2H), 1.02-1.12 (m, 2H), 1.17 (d, J = 6.3 Hz, 3H), 1.17 (br s, 1H), 1.47 (ddd, J = 4.8, 8.1, 12.6 Hz, 1H), 2.32 (br s, 1H), 4.73-4.86 (m, 1H), 5.68 (br s, 1H), 6.45 (d, J = 7.8 Hz, 1H), 6.89 (t, J = 6.9 Hz, 1H), 7.14-7.39 (m, 12H).

ESIMS *m/z*: $[M+H]^+$ 411.

EXAMPLE 13

N-[(2*S**, 4*R**)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclobutanecarboxamide (Compound 3-3)

The compound, (2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline, obtained in Reference 1 was reacted with cyclobutanecarbonyl chloride to created Compound 3-3.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.15 (d, J = 6.3 Hz, 3H), 1.52-1.57 (m, 1H), 1.75-1.97 (m, 4H), 2.30 (br s, 1H), 2.37-2.53 (m, 2H), 3.15 (quin, J = 8.5 Hz, 1H), 4.75-4.83 (m, 1H), 5.60 (br s, 1H), 6.49 (dd, J = 1.1, 7.9 Hz, 1H), 6.89 (t, J = 7.3 Hz, 1H), 7.12-7.39 (m, 12H).

ESIMS *m/z*: $[M+H]^+$ 425.

EXAMPLE 14

N-[(2*S**, 4*R**)-1-(4-fluorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-5)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 4-fluorobenzoic acid chloride to created Compound 3-5.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.71-0.76 (m, 2H), 1.07-1.17 (m, 3H), 1.16 (d, J = 6.3 Hz, 3H), 1.42-1.51 (m, 1H), 2.31 (br s, 1H), 4.70-4.80 (m, 1H), 5.64 (br s, 1H), 6.47 (d, J = 7.9 Hz, 1H), 6.82-6.95 (m, 3H), 7.16-7.22 (m, 3H), 7.34-7.40 (m, 6H).

ESIMS *m/z*: $[M+H]^+$ 429.

EXAMPLE 15

N-[(2*S**, 4*R**)-1-(4-methylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-6)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 4-methylbenzoic acid chloride to created Compound 3-6.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.71-0.74 (m, 2H), 1.08-1.26 (m, 3H), 1.15 (d, J = 6.1 Hz, 3H), 1.42-1.51 (m, 1H), 2.27 (s, 3H), 2.31 (br s, 1H), 4.72-4.81 (m, 1H), 5.65 (br s, 1H), 6.50 (d, J = 7.7 Hz, 1H), 6.91 (t, J = 7.8 Hz, 1H), 6.97 (d, J = 7.9 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 7.17 (t, J = 7.6 Hz, 1H), 7.33-7.50 (m, 6H).

ESIMS *m/z*: $[M+H]^+$ 425.

EXAMPLE 16

N-[(2*S**, 4*R**)-1-(4-chlorobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-12)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 4-chlorobenzoic acid chloride to created Compound 3-12.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.71-0.75 (m, 2H), 1.07-1.17 (m, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.42-1.51 (m, 1H), 2.31 (br s, 1H), 4.70-4.80 (m, 1H), 5.64 (br s, 1H), 6.48 (d, *J* = 7.8 Hz, 1H), 6.93 (t, *J* = 6.9 Hz, 1H), 7.14-7.40 (m, 1H).
ESIMS *m/z*: $[M+H]^+$ 445.

EXAMPLE 17

N-[(2*S**, 4*R**)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-13)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 4-bromobenzoic acid chloride to created Compound 3-13.
^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.71-0.75 (m, 2H), 1.07-1.17 (m, 3H), 1.16 (d, *J* = 6.3 Hz, 3H), 1.42-1.50 (m, 1H), 2.31 (br s, 1H), 4.72-4.80 (m, 1H), 5.64 (br s, 1H), 6.47 (d, *J* = 7.8 Hz, 1H), 6.94 (t, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 8.7 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.30-7.40 (m, 8H).
ESIMS *m/z*: $[M+H]^+$ 490.

EXAMPLE 18

N-[(2*S**, 4*R**)-1-(4-methoxycarbonylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-17)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with monoethyl ester terephthalate chloride to created Compound 3-17.
^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.72-0.75 (m, 2H), 1.08-1.18 (m, 3H), 1.17 (d, *J* = 6.0 Hz, 3H), 1.44-1.49 (m, 1H), 1.59 (s, 3H), 2.32 (br s, 1H), 4.74-4.84 (m, 1H), 5.67 (br s, 1H), 6.44 (d, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 7.7 Hz, 1H), 7.15-7.40 (m, 9H), 7.85 (d, *J* = 7.8 Hz, 1H),.
ESIMS *m/z*: $[M+H]^+$ 469.

EXAMPLE 19

N-[(2*S**, 4*R**)-1-(4-carboxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-18)

The compound, N-[(2*S**, 4*R**)-1-(4-methoxycarbonylbenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Example 13 was dissolved in methanol (5 ml), and sodium hydroxide solution (15 %, 1.0 ml) and tetrahydrofuran (1.0 ml) were added to the mixture. The mixture was stirred for two hours at 45 degrees Celsius. After the solvent was distilled under a reduced pressure, the solution was acidified by adding hydrochloride (3 mol/l). The deposited crystal was filtered out and Compound 3-18 (947 mg) was obtained.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.67-0.71 (m, 2H), 0.82-0.93 (m, 2H), 1.04 (d, J = 6.2 Hz, 3H), 1.34 (br s, 1H), 2.46 (br s, 1H), 4.60-4.69 (m, 1H), 5.52 (br s, 1H), 6.51 (d, J = 8.1 Hz, 1H), 6.91 (t, J = 7.6 Hz, 1H), 7.15-7.48 (m, 9H), 7.76 (d, J = 8.4 Hz, 2H), 13.11 (s, 1H).

ESIMS *m/z*: $[M+H]^+$ 455.

EXAMPLE 20

N-{(2*S**, 4*R**)-2-methyl-1-[4-(N-methylaminocarbonyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide (Compound 3-20)

The compound, N-[(2*S**, 4*R**)-1-(4-carboxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (70 mg), obtained in Example 14, hydroxybenzotriazol (120 mg), methylamine hydrochloride (52 mg), and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimido hydrochloride (50 mg) were dissolved in DMF (5 ml), and triethylamine (0.21 ml) was added to the mixture. The mixture was stirred for 12 hours at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture, and the mixture was eluted with ethyl acetate. After distilling the solvent under a reduced pressure, the residue was refined by preparative thin layer chromatography (ethyl acetate) to obtain Compound 3-20 (55 mg).

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.72-0.75 (m, 2H), 1.07-1.18 (m, 3H), 1.17 (d, J = 6.3 Hz, 3H), 1.43-1.48 (m, 1H), 2.31 (br s, 1H), 2.96-2.99 (m, 3H), 4.75-4.83 (m, 1H), 5.68 (br s, 1H), 6.44 (d, J = 7.5 Hz, 1H), 6.87 (t, J = 7.7 Hz, 1H), 7.15-7.58 (m, 11H).

ESIMS *m/z*: $[M+H]^+$ 488.

EXAMPLE 21

N-{(2*S**, 4*R**)-1-[4-(N, N-dimethylaminocarbonyl)benzoyl]-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide (Compound 3-21)

The compound, N-[(2*S**, 4*R**)-1-(4-carboxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Example 14 was reacted with dimethylamine chloride to create Compound 3-21.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.72-0.75 (m, 2H), 1.07-1.18 (m, 3H), 1.17 (d, J = 6.3 Hz, 3H), 1.43-1.49 (m, 1H), 2.31 (br s, 1H), 2.86 (s, 3H), 3.07 (s, 3H), 4.75-4.83 (m, 1H), 5.67 (br s, 1H), 6.48 (d, J = 8.1 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 7.16-7.40 (m, 11H).

ESIMS *m/z*: $[M+H]^+$ 482.

EXAMPLE 22

N-[(2*S**, 4*R**)-1-(3-methoxybenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-25)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 3-methoxybenzoic acid chloride to create Compound 3-25.

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.72-0.74 (m, 2H), 1.03-1.17 (m, 3H), 1.16 (d, J = 6.2 Hz, 3H), 1.41-1.51 (m, 1H), 2.32 (br s, 1H), 3.66 (s, 3H), 4.72-4.85 (m, 1H), 5.63 (br s, 1H), 6.53 (d, J = 7.8 Hz, 1H), 6.67 (t, J = 7.6 Hz, 1H), 6.76-6.83 (m, 1H), 6.86 (s, 1H), 6.91 (t, J = 7.6 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 7.17 (t, J = 7.3 Hz, 1H), 7.34-7.39 (m, 6H).

ESIMS *m/z*: $[M+H]^+$ 441.

EXAMPLE 23

N-[(2*S**, 4*R**)-2-methyl-1-(3-methylbenzoyl)-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-33)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 3-methylbenzoic acid chloride to create Compound 3-33.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 0.70-0.78 (m, 2H), 1.05-1.16 (m, 3H), 1.15 (d, J = 6.6 Hz, 3H), 1.42-1.50 (m, 1H), 2.27 (s, 3H), 2.32 (br s, 1H), 4.74-4.84 (m, 1H), 5.66 (br s, 1H), 6.50 (dd, J = 7.8, 0.9 Hz, 1H),

6.78 (d, J = 7.2 Hz, 1H), 6.90 (t, J = 7.5 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 7.07 (d, J = 7.8 Hz, 1H), 7.16 (td, J = 7.8, 1.2 Hz, 1H), 7.23 (s, 1H), 7.35-7.39 (m, 6H).
ESIMS m/z: $[M+H]^+$ 425.

EXAMPLE 24

N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylthio)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide (Compound 3-34)

The compound, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide, obtained in Reference 2 was reacted with 3-methylthiobenzoic acid chloride to create Compound 3-34.
^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.71-0.75 (m, 2H), 1.07-1.18 (m, 3H), 1.15 (d, J = 6.2 Hz, 3H), 1.42-1.51 (m, 1H), 2.32 (br s, 1H), 2.41 (s, 3H), 4.69-4.82 (m, 1H), 5.66 (br s, 1H), 6.52 (dd, J = 8.1 Hz, 1H), 6.90-7.40 (m, 12H).
ESIMS m/z: $[M+H]^+$ 457.

EXAMPLE 25

N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylsulfinyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide (Compound 3-35)

The compound, N-[(2*S**, 4*R**)-1-(4-methylthiobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (50 mg), obtained in Example 21 was dissolved in chloroform (10 ml), meta-chloroperbenzoic acid chloride (18 mg) was added to the mixture, and stirred for one hour at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture, and the solvent was distilled under a reduced pressure and eluted with ethyl acetate. After refining with preparative thin layer chromatography (chloroform:methanl = 25:1), the residue was recrystallized with hexane-ethyl acetate to obtain Compound 3-35 (43 mg).
^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.72-0.76 (m, 2H), 1.07-1.19 (m, 3H), 1.18 (d, J = 6.3 Hz, 3H), 1.43-1.51 (m, 1H), 2.32 (br s, 1H), 2.65-2.66 (m, 3H), 4.76-4.84 (m, 1H), 5.66 (br s, 1H), 6.45 (d, J = 7.8 Hz, 1H), 6.86-6.93 (m, 1H), 7.17-7.49 (m, 11H).
ESIMS m/z: $[M+H]^+$ 473.

EXAMPLE 26

N-{(2*S**, 4*R**)-2-methyl-1-[4-(methylsulphonyl)benzoyl]-1,2,3,4-tetrahydroquinoline-4-yl}-N-phenylcyclopropanecarboxamide (Compound 3-36)

The compound, N-[(2*S**, 4*R**)-1-(4-methylthiobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (50 mg), obtained in Example 21 was dissolved in chloroform (10 ml), meta-chloroperbenzoic acid chloride (50 mg) was added to the mixture, and stirred for one hour at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture, and the solvent was distilled under a reduced pressure and eluted with ethyl acetate. After refining with silica gel column chromatography (hexane:ethyl acetate = 2:1), the residue was recrystallized with hexane-ethyl acetate to obtain Compound 3-36 (33 mg).

^{1}H-NMR (270 MHz, $CDCl_3$, δ): 0.73-0.77 (m, 2H), 1.06-1.18 (m, 3H), 1.19 (d, J = 6.0 Hz, 3H), 1.43-1.51 (m, 1H), 2.31 (br s, 1H), 2.99 (m, 3H), 4.74-4.86 (m, 1H), 5.66 (br s, 1H), 6.43 (d, J = 7.8 Hz, 1H), 6.91 (t, J = 6.9 Hz, 1H), 6.55-7.42 (m, 9H), 7.75-7.79 (m, 2H).

ESIMS *m/z*: $[M+H]^+$ 489.

EXAMPLE 27

N-[(2*S*, 4*R*)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-37) and N-[(2*R*, 4*S*)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (Compound 3-38)

Optical isomers of N-[(2*S**, 4*R**)-1-(4-bromobenzoyl)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (100 mg) were separated by a chiral HPLC column (Daicel Chorale OD; 2-propanol:hexane = 1:9; flow rate: 5 ml/ min.; detected wavelength: 254 nm), and a mirror image isomer (38 mg) with a retention time of 27.39 minutes and a mirror image isomer (6 mg) with a retention time of 35.87 minutes were obtained.

REFERENCE 1

(2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline

Under a dry nitrogen atmosphere, methylene chloride (150 ml) solution of (2*S**, 4*R**)-4-(N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline (Canadian Journal of Chemistry (Can. J. Chem.), vol.

42, p. 2885 (1969)) (15.0 g, 62.9 mmol) and pyridine (150 ml) was prepared and cooled to 0 degrees Celsius. At 0 degrees Celsius, benzoyl chloride (7.30 ml, 63.0 mmol) was very slowly added while stirring the mixture. After stirring for 30 minutes at the same temperature, benzoyl chloride (1.50 ml, 12.9 mmol) was added, and the mixture was stirred for 10 minutes at 0 degrees Celsius and further stirred for one hour at room temperature. Saturated sodium hydrogen carbonate solution was added to the reaction mixture, and the solvent was distilled under a reduced pressure. Saturated sodium hydrogen carbonate solution was added to the residue, the mixture was eluted with chloroform, and the organic layer was washed with hydrochloride (1 mol/l, 100 ml). After organic solvent was distilled under a reduced pressure, the residue was subjected to silica gel column chromatography (hexane:ethyl acetate = 1:1, and then hexane:ethyl acetate:chloroform = 45:45:10) to remove highly polar components. The residue was recrystallized with hexane-ethyl acetate, and the final product, (2*S**, 4*R**)-4-(N-phenylamino)-1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinoline (20.5 g, 95.1 %), was obtained as a white crystal.
^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.29 (d, *J* = 6.0 Hz, 3H), 1.46-1.33 (m, 1H), 2.82 (ddd, *J* = 4.5, 8.7, 13.5 Hz, 1H), 3.89 (d, *J* = 7.2 Hz, 1H), 4.44-4.52 (m, 1H), 4.87-4.99 (m, 1H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 2H), 6.79 (dd, *J* = 7.2, 7.5 Hz, 1H), 6.91 (t, *J* = 7.8 Hz, 1H), 7.06 (dd, *J* = 7.5, 7.8 Hz, 1H), 7.20-7.35 (m, 8H).

REFERENCE 2

N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide

In a pressure-resistant container, the compound, N-[(2*S**, 4*R**)-1-benzyloxycarbonyl-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylpropanecarboxamide (7.58 g), obtained in Example 12 was dissolved in ethanol (100 ml), and formic acid (7.58 ml) and palladium carbon (10 % Pd-C, 2.0 g) were added to the mixture. After replacing the atmosphere in the container with nitrogen, the atmosphere was further replace with hydrogen gas. Keeping 3.0 MPa pressure of the hydrogen gas, the mixture was stirred for four hours at 45 degrees Celsius. The palladium carbon was filtered out from the reaction mixture and the solvent was distilled under a reduced pressure. Saturated sodium hydrogen carbonate solution was added to the mixture, and the mixture was eluted with ethyl acetate. After distilling the organic solvent under a reduced pressure, the residue was crystallized with hexane-ethyl acetate, and the final product, N-[(2*S**, 4*R**)-2-methyl-1,2,3,4-tetrahydroquinoline-4-yl]-N-phenylcyclopropanecarboxamide (5.1 g, 97 %), was obtained as a colorless crystal.
ESIMS *m/z*: $[M+H]^+$ 307.

REFERENCE 3

(2*S**, 4*R**)-4-(N-phenylamino)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline

Under a dry nitrogen atmosphere, methylene chloride (50 ml) solution of (2*S**, 4*R**)-4-(N-phenylamino)-2-methyl-1,2,3,4-tetrahydroquinoline (Canadian Journal of Chemistry (Can. J. Chem.), vol. 42, p. 2885 (1969)) (5.4 g) and pyridine (50 ml) was prepared and cooled to 0 degrees Celsius. 2-furoyl chloride (2.2 ml) was added to the mixture while stirring. After stirring for two hours at 0 degrees Celsius, saturated sodium hydrogen carbonate solution was added, and the solvent was distilled under a reduced pressure. Saturated sodium hydrogen carbonate solution was added to the residue, the mixture was eluted with chloroform, and the organic layer was washed with hydrochloride (3 mol/l, 20 ml) and saturated sodium hydrogen carbonate solution (20 ml). After organic solvent was distilled under a reduced pressure, the residue was purified by silica gel column chromatography (hexane:ethyl acetate:chloroform = 45:45:10). The residue was recrystallized with hexane-ethyl acetate, and the final product, (2*S**, 4*R**)-4-(N-phenylamino)-1-(2-furoyl)-2-methyl-1,2,3,4-tetrahydroquinoline (5.3 g), was obtained as a white crystal.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 1.27 (d, J = 6.0 Hz, 3H), 1.30-1.41 (m, 1H), 2.73-2.79 (m, 1H), 3.87 (br s, 1H), 4.37-4.42 (m, 1H), 4.80-4.90 (m, 1H), 6.33 (dd, J = 3.3, 1.5 Hz, 1H), 6.43 (dd, J = 3.3, 0.6 Hz, 1H), 6.65-6.89 (m, 4H), 7.09-7.38 (m, 6H).

REFERENCE 4

4-(N-phenylamino)-1-benzoyl-1,2,3,4-tetrahydroquinoline

PROCESS 1

3-(N-benzoyl-N-phenylamino)propionic acid

Acetate (10 ml) and water (10 ml) was added to aniline (20 g) and ethyl acrylate (21 ml) and heat refluxed for 12 hours. After left standing to cool down to room temperature, chloroform (200 ml) was added to remove the aqueous layer, and the chloroform layer was washed with hydrochloride (1 mol/l) and saturated sodium hydrogen carbonate solution. Pyridine (13 ml) and chloroform (100 ml) were added to the residue, which was obtained by distilling the solvent. Benzoic acid chloride (23 ml) was added slowly at 0 degrees Celsius, and the mixture was stirred for two hours at 0 degrees Celsius, further stirred for two hours at room temperature. After the solvent was distilled under a reduced pressure, saturated

sodium hydrogen carbonate solution was added to the mixture, and the mixture was eluted with chloroform. After distilling the organic layer under a reduced pressure, highly polar components were removed using silica gel. The residue obtained by distilling the solvent was dissolved in methanol (100 ml), and sodium hydroxide solution (15 %, 50 ml) was added to the solution. The solution was stirred for two hours at room temperature. After adding toluene (100 ml) and stirring the mixture, the aqueous layer was separated, and hydrochloride (3 mol/l) was added to acidify the mixture. Precipitated crystals were filtered out and dried under a reduced pressure to obtain the final product, 3-(N-benzoyl-N-phenylamino)propionic acid (30 g).

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 2.76 (t, J = 7.4 Hz, 2H), 4.23 (t, J = 7.4 Hz, 2H), 7.03-7.30 (m, 10H).

PROCESS 2

1-benzoyl-2,3-dihydroquinoline-4-ones

The compound, 3-(N-benzoyl-N-phenylamino)propionic acid (2.0 g), obtained in Process 2 was dissolved in methylene chloride (10 ml), and thionyl chloride (1.5 ml) was added to the mixture. After stirring for four hours at room temperature, the solvent was distilled, and the residue was dissolved again in methylene chloride (10 ml). Methylene chloride (4 ml) was added to aluminum chloride (2 g), and the methylene chloride solution prepared above was titrated at room temperature. After stirring for one hour without changing the temperature, the reaction mixture was added to ice water, and eluted with chloroform. The organic layer was washed with hydrochloride (1 mol/l) as well as saturated sodium hydrogen carbonate solution, and the solvent was distilled under a reduced pressure. The final product, 1-benzoyl-2,3-dihydroquinoline-4-ones (1.8 g), was obtained by recrystallizing the residue with ethanol.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 2.89 (t, J = 6.3 Hz, 2H), 4.33 (t, J = 6.3 Hz, 2H), 6.91 (d, J = 8.1 Hz, 1H), 7.13-7.50 (m, 7H), 8.00 (dd, J = 7.8, 1.8 Hz, 1H).

ESIMS m/z: $[M+H]^+$ 252.

PROCESS 3

4-(N-phenylamino)-1-benzoyl-1,2,3,4-tetrahydroquinoline

Molecular sieves 3A (9 g), para-toluene sulfonic acid (10 mg), aniline (0.55 ml) and toluene (50 ml) were added to the compound, 1-benzoyl-2,3-dihydroquinoline-4-ones (360 mg), obtained in Process 2, and heat refluxed for 12 hours. After left standing to cool down to room temperature, chloroform was added, molecular sieves 3A was filtered out, and the solvent was distilled under a reduced pressure. Methanol (20 ml) and sodium borohydride (1.0 g) was added to the mixture, and stirred for 12 hours at

room temperature. After adding saturated sodium hydrogen carbonate solution, the solvent was distilled under a reduced pressure, and eluted with ethyl acetate. The residue obtained by distilling the solvent was recrystallized by ethyl acetate-hexane, and the final product, 4-(N-phenylamino)-1-benzoyl-1,2,3,4-tetrahydroquinoline (210 mg), was obtained.

^{1}H-NMR (300 MHz, $CDCl_3$, δ): 2.00-2.11 (m, 1H), 2.30-2.40 (m, 1H), 3.68-3.77 (m, 1H), 3.96 (br s, 1H), 4.17-4.25 (m, 1H), 4.64 (br s, 1H), 6.69-7.42 (m, 14H).

ESIMS *m/z*: $[M+H]^+$ 329.

EXAMPLE 28: Tablet

Using an ordinary method, tablet having the following composition is prepared:

Formula:	Compound 43	20	mg
	Lactose	143.4	mg
	Potato starch	30	mg
	Hydroxypropylcellulose	6	mg
	Magnesium stearate	0.6	mg
		200	mg

EXAMPLE 29: Injection

Using an ordinary method, injection having the following composition is prepared:

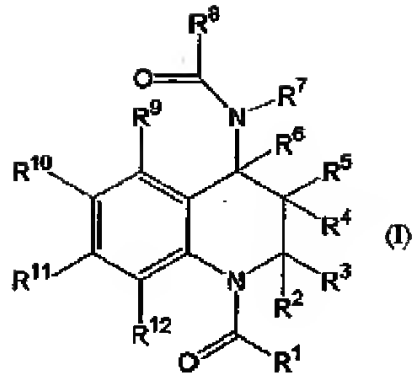
Formula:	Compound 43	2	mg
	Refined soybean oil	200	mg
	Refined egg-yolk lecithin	24	mg
	Glycerin for injection	50	mg
	Distilled water for injection	1.72	ml
		2.00	ml

Industrial Availability

The present invention enables to offer an anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative, or 4-aminotetrahydroquinoline derivatives or a pharmacologically acceptable salt of the derivatives having an anti-inflammatory activity.

What is claims is:

1. Formula (I)



(I)

An anti-inflammatory agent which contains as an active ingredient either a 4-aminotetrahydroquinoline derivative represented by the formula (I):

(wherein R^1 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, $CONR^AR^B$ (wherein R^A and R^B are the same or different and each represents hydrogen or substituted or unsubstituted lower alkyl, but R^A and R^B do not represent hydrogen at the same time), or NR^CR^D (wherein R^C and R^D are the same or different and each represents hydrogen, substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower aryl);

R^2 and R^3 are the same or different and each represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as R^A and R^B above);

R^4 and R^5 are the same or different and each represents hydrogen, halogen, nitro, hydroxyl, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or

unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, $CONR^{A2}R^{B2}$ (wherein R^{A2} and R^{B2} have the same meaning as R^A and R^B above), $NR^{C1}R^{D1}$ (wherein R^{C1} and R^{D1} have the same meaning as R^C and R^D above), OR^E (wherein R^E represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted aromatic heterocyclic group), or $S(O)_nR^F$ (wherein *n* represents an integer 0 to 2 and R^F represents substituted or unsubstituted lower alkyl);

R^6 represents hydrogen, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A3}R^{B3}$ (wherein R^{A3} and R^{B3} have the same meaning as R^A and R^B above);

R^7 represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;

R^9, R^{10}, R^{11} and R^{12} are the same or different and each represents hydrogen, halogen, nitro, hydroxyl, mercapto, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, $CONR^{A4}R^{B4}$ (wherein R^{A4} and R^{B4} have the same meaning as R^A and R^B above), $NR^{C2}R^{D2}$ (wherein R^{C2} and R^{D2} have the same meaning as R^C and R^D above), OR^{E1} (wherein R^{E1} has the same meaning as R^E above), or $S(O)_{n1}R^{F1}$ (wherein *n*1 and R^{F1} have the same meaning as *n* and R^F above);

1-1) When R^1 represents lower alkyl or halogen-substituted lower alkyl;

1-1-1) and R^2 and R^3 above are the same or different and each represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above) (when, however, either one of R^2 or R^3 represents lower alkyl or halogen-substituted lower alkyl, the other one of R^2 or R^3 does not represent hydrogen);

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as R^A and R^B above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as R^C and R^D above);

1-1-2) and either one of R^2 or R^3 represents lower alkyl or halogen-substituted lower alkyl, the other one of R^2 or R^3 represents hydrogen; and

1-1-2-1) R^7 represents substituted or unsubstituted cycloalkyl or substituted or unsubstituted alicyclic heterocyclic group;

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above);

1-1-2-2) R^7 represents substituted or unsubstituted aryl or substituted or unsubstituted aromatic heterocyclic group;

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above);

1-2) When R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, $CONR^AR^B$ (wherein R^A and R^B have the same meaning as above), or NR^CR^D (wherein R^C and R^D have the same meaning as above);

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, $CONR^{A5}R^{B5}$ (wherein R^{A5} and R^{B5} have the same meaning as above), or $NR^{C3}R^{D3}$ (wherein R^{C3} and R^{D3} have the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

2. An anti-inflammatory agent as set forth in 1 above wherein R^4 and R^5 are hydrogen.

3. An anti-inflammatory agent as set forth in 1 or 2 above wherein R^6 is hydrogen.

4. An anti-inflammatory agent as set forth in 1 above wherein R^1 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d are the same or different and each represents hydrogen, substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower aryl, but do not represent hydrogen at the same time);
R^3, R^4, R^5 and R^6 each represents hydrogen;
At least two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen;
4-1) R^1 represents lower alkyl or halogen-substituted lower alkyl; and

4-1-1) R^2 represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted

or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as R^c and R^d above); or

4-1-2) R^2 represents lower alkyl or halogen-substituted lower alkyl;

4-1-2-1) R^7 represents substituted or unsubstituted cycloalkyl or substituted or unsubstituted alicyclic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); or

4-1-2-2) R^7 represents substituted or unsubstituted aryl or substituted or unsubstituted aromatic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); or

4-2) R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d have the same meaning as above);

R^2 represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted heterocyclic group, or $CONR^{A1}R^{B1}$ (wherein R^{A1} and R^{B1} have the same meaning as above); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted

or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above).

5. An anti-inflammatory agent as set forth in 1 above wherein R^2 represents hydrogen, substituted or unsubstituted lower alkyl;

R^3, R^4, R^5 and R^6 each represents hydrogen;

R^7 represents substituted or unsubstituted aryl;

At least two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen, the other two are the same or different, and each represents hydrogen, halogen, nitro, hydroxyl, lower alkyl, substituted or unsubstituted lower alkoxy; and

5-1) R^1 represents lower alkyl or halogen-substituted lower alkyl;

5-1-1) R^2 represents hydrogen, or substituted lower alkyl (excluding halogen-substituted lower alkyl); and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; or

5-1-2) R^2 represents lower alkyl or halogen-substituted lower alkyl; and

R^8 represents hydrogen, substituted or unsubstituted lower cycloalkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; or

5-2) R^1 represents hydrogen, substituted lower alkyl (excluding halogen-substituted lower alkyl), substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group; and

R^8 represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted arylamino, or substituted or unsubstituted aromatic heterocyclic group.

6. An anti-inflammatory agent as set forth in 1, 2, or 3 above wherein R^9, R^{10}, R^{11} and R^{12} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^{E1} (wherein R^{E1} has the same meaning as above).

7. An anti-inflammatory agent as set forth in 4 above wherein two of R^9, R^{10}, R^{11} and R^{12} represent hydrogen, and the other two are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkylthio, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^{E1} (wherein R^{E1} has the same meaning as above).

8. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S**, 4*R**), respectively.

9. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R**, 4*R**), respectively.

10. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*R*), respectively.

11. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*S*), respectively.

12. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*R*), respectively.

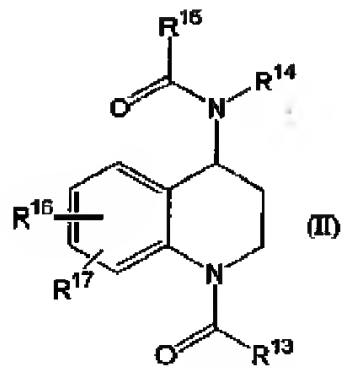
13. An anti-inflammatory agent as set forth in 1, 2, 3, 4, 5, 6, or 7 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*S*), respectively.

14. Usage of a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 above for the purpose of manufacturing an anti-inflammatory agent.

15. A prevention and/ or a method for the treatment of inflammation which comprises the step to administer an effective dose of either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 above.

16. A pharmaceutical composition having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 above.

17. Formula (II)



(II)

Either a 4-aminotetrahydroquinoline derivative represented by the formula (II):

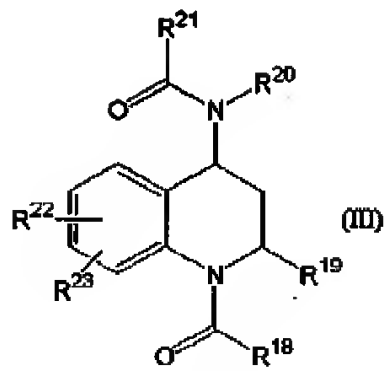
(wherein R^{13} represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkoxycarbonylamino, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted lower alkanoylamino, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aralkyloxy, substituted or unsubstituted heterocyclic group, or NR^cR^d (wherein R^c and R^d have the same meaning as above);

R^{14} represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;

R^{15} represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heterocyclic group, or $NR^{c1}R^{d1}$ (wherein R^{c1} and R^{d1} have the same meaning as above); and

R^{16} and R^{17} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^E (wherein R^E has the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

18. Formula (III)



(III)

A 4-aminotetrahydroquinoline derivative represented by the formula (III):

(wherein R^{18} represents substituted or unsubstituted aryl;

R^{19} represents hydrogen, cyano, carboxy, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted lower

alkoxycarbonyl, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl, substituted or unsubstituted aroyl, substituted or unsubstituted aromatic heterocyclic group, or $CONR^AR^B$ (wherein R^A and R^B have the same meaning as above);
R^{20} represents substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or substituted or unsubstituted heterocyclic group;
R^{21} represents substituted or unsubstituted cycloalkyl;
R^{22} and R^{23} are the same or different and each represents hydrogen, halogen, amino, nitro, cyano, lower alkyl, aryloxy lower alkyl, heterocyclic lower alkyl, aromatic heterocyclicoxy lower alkyl, lower alkenyl, lower alkynyl, aralkyl, heterocyclic group, substituted or unsubstituted styryl, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted alkanoyl, substituted or unsubstituted aryl, substituted or unsubstituted aroyl, or OR^E (wherein R^E has the same meaning as above)) or a pharmacologically acceptable salt of the derivative.

19. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18 above wherein R^{19} represents substituted or unsubstituted lower alkyl, and R^{22} and R^{23} each represents hydrogen.

20. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18 or 19 above wherein R^{19} represents methyl.

21. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19 or 20 above wherein R^{20} represents substituted or unsubstituted phenyl.

22. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S**, 4*R**), respectively.

23. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein a relative configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R**, 4*R**), respectively.

24. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*R*), respectively.

25. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*S*), respectively.

26. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*R*, 4*R*), respectively.

27. A 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 18, 19, 20 or 21 above wherein an absolute configuration of 2- and 4-position in the tetrahydroquinoline skeleton of a 4-aminotetrahydroquinoline derivative is (2*S*, 4*S*), respectively.

28. An anti-inflammatory agent having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative set forth in 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27 above.

29. Usage of a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27 above for the purpose of manufacturing an anti-inflammatory agent.

30. A prevention and/ or a method for the treatment of inflammation which comprises the step to administer an effective dose of either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27 above.

31. A pharmaceutical composition having as an active ingredient either a 4-aminotetrahydroquinoline derivative or a pharmacologically acceptable salt of the derivative as set forth in 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, or 27 above.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/15608

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07D215/44, 221/14, 401/06, 401/12, 401/14, 405/06, 405/14, 409/06, 409/14, A61K31/4706, 31/4709, A61P1/02, 1/04, 3/10, 5/14, 7/00, 7/02, 9/00, 9/10, 9/14, 11/00, 11/02,
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07D215/44, 221/14, 401/06, 401/12, 401/14, 405/06, 405/14, 409/06, 409/14, A61K31/4706, 31/4709, A61P1/02, 1/04, 3/10, 5/14, 7/00, 7/02, 9/00, 9/10, 9/14, 11/00, 11/02,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN/CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/19755 A1 (SMITH-KLINE BEECHAM PLC.), 14 October, 1993 (14.10.93), In general formula(I), X_1:NR^0, R^0: alkylcarbonyl, R_4: hydrogen, R_5: formula(a), A:>C=O, R_6: hydrogen, alkyl, aryl, heterocyclic compound & AU 3765193 A & GB 9207400 A & CA 2133470 A & MX 9301879 A & ZA 9302303 A & EP 633778 A & JP 7-505381 A	1-29,31
P,X	WO 03/105849 A1 (RHEOGENE, INC.), 24 December, 2003 (24.12.03), (Family: none)	1-27,31

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 February, 2004 (10.02.04)	24 February, 2004 (24.02.04)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/15608

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00/017165 A1 (Pfizer Products Inc.), 30 March, 2000 (30.03.00), & BR 9913855 A & EE 200100167 A & US 6489478 B1 & ZA 2001001745 A & NO 2001001349 A & HR 2001000200 A & BR 105429 A & JP 2002-526476 A	1-27,31

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/15608

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 30

because they relate to subject matter not required to be searched by this Authority, namely:

The invention as set forth in claim 30 pertains to methods for treatment of the human body by therapy.

2. [ ] Claims Nos.:

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4 [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest [ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP03/15608

Continuation of A. CLASSIFICATION OF SUBJECT MATTER
(International Patent Classification (IPC))

Int.Cl[7] 11/06, 13/12, 17/00, 17/02, 17/04, 17/06, 21/00, 21/04, 25/00, 25/02, 25/04, 25/28, 27/02, 29/00, 29/02, 31/04, 31/10, A61P33/02, 35/00, 35/02, 35/04, 37/04, 37/06, 37/08, 43/00

(According to International Patent Classification (IPC) or to both national classification and IPC)

Continuation of B. FIELDS SEARCHED
Minimum Documentation Searched(International Patent Classification (IPC))

Int.Cl[7] 11/06, 13/12, 17/00, 17/02, 17/04, 17/06, 21/00, 21/04, 25/00, 25/02, 25/04, 25/28, 27/02, 29/00, 29/02, 31/04, 31/10, A61P33/02, 35/00, 35/02, 35/04, 37/04, 37/06, 37/08, 43/00

Minimum documentation searched (classification system followed by classification symbols)

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/JP03/15608

A. CLASSIFICATION OF SUBJECT MATTER (International Search Report (IPC))
Int.Cl[7] C07D215/44, 221/14, 401/06, 401/12, 401/14, 405/06, 405/14, 409/06, 409/14, A61K31/4706, 31/4709, A61P1/02, 1/04, 3/10, 5/14, 7/00, 7/02, 9/00, 9/10, 9/14, 11/00, 11/02, 11/06, 13/12, 17/00, 17/02, 17/04, 17/06, 21/00, 21/04, 25/00, 25/02, 25/04, 25/28, 27/02, 29/00, 29/02, 31/04, 31/10,

B. FIELDS SEARCHED

Minimum documentation searched (International Search Report (IPC))
Int.Cl[7] C07D215/44, 221/14, 401/06, 401/12, 401/14, 405/06, 405/14, 409/06, 409/14, A61K31/4706, 31/4709, A61P1/02, 1/04, 3/10, 5/14, 7/00, 7/02, 9/00, 9/10, 9/14, 11/00, 11/02, 11/06, 13/12, 17/00, 17/02, 17/04, 17/06, 21/00, 21/04, 25/00, 25/02, 25/04, 25/28, 27/02, 29/00, 29/02, 31/04, 31/10,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
STN/CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93/19755 A1 (SMITH-KLINE BEECAHM PLC), 14 October, 1993 In general formula (I), Y_1: NR^0, R^0: alkylcarbonyl, R_4: hydrogen, R_5: formula (a), A: > C = O, R_6: hydrogen, alkyl, aryl, heterocyclic compound & AU 3765193 A & GB 9207400 A & CA 2133470 A & MX 9301879 A & ZA 9302303 A & EP 633778 A & JP 7-505381 A	1-29, 31

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A": documents defining the general state of the art which is not considered to he of particular relevance

"E": earlier document but published on or after the international filing date

"L": document which may throw douhts on priority claim(s) or which is cited to establish the puhlication date of another citation or other special reason (as specified)

"O": document referring to an oral disclosure, use, exhibition or other means

"P": document published prior to the international filing date but later than the priority date claimed

"T": later document puhlished after the international filing date or priority date and not in conflict with the application hut cited to understand the principle or theory underlying the invention

"X": document of particular relevance; the claimed invention cannot be considered novel or cannot he considered to involve an inventive step when the document is taken alone

"Y": document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&": document member of the same patent family

Date of the actual completion of the international search
10 February, 2004 (10.02.04)

Date of mailing of the international search report
24 February, 2004 (24.02.04)

Name and mailing address of the ISA/JP
Japanese Patent Office (ISA/JP)
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Japan,100-8915

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Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International Application No. PCT/JP03/15608

C (Continuation). DOCUMENTS CONSDIERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	WO 03/105849 A1 (RHEOGENE, INC.), 24 December, 2003 (24.12.03) (Family: none)	1-27, 31
X	WO 00/017165 A1 (Pfizer Products, Inc.), 30 March, 2000 (30.03.00), & BR 9913855 A & EE 200100167 A & US 6489478 B1 & ZA 2001001745 A & NO 2001001349 A & HR 2001000200 A & BG 105429 A & JP 2002-526476 A	1-27, 31

INTERNATIONAL SEARCH REPORT

International Application No. PCT/JP03/15608

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 8, section 3 of the Japan Patent Law (PCT, Article 17(2)(a)) for the following reasons:

1. ☒ Claims Nos.: 30 , because they relate to subject matter not required to be searched by this Authority, namely:
The invention as set forth in claim 30 pertains to methods for treatment of the human body by therapy.

2. ☐ Claims Nos.:___ , because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. ☐ Claims Nos.:___ , because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).:

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest on Additional Search Fees

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/JP03/15608

Continuation of A. CLASSIFICATION OF SUBJECT MATTER
(International Patent Classification (IPC))
A61P33/02, 35/00, 35/02, 35/04, 37/04, 37/06, 37/08, 43/00

Continuation of B. FIELDS SEARCHED
A61P33/02, 35/00, 35/02, 35/04, 37/04, 37/06, 37/08, 43/00